IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AKEBIA THERAPEUTICS, INC. and OTSUKA AMERICA PHARMACEUTICAL, INC., Plaintiffs, v. FIBROGEN, INC. and ASTRAZENECA AB, Defendants.	Civil Action No. _____

COMPLAINT FOR DECLARATORY JUDGMENT
OF PATENT INVALIDITY AND NONINFRINGEMENT

Plaintiffs Akebia Therapeutics, Inc. ("Akebia") and Otsuka America Pharmaceutical, Inc. ("Otsuka America") (collectively, "Plaintiffs"), by their undersigned counsel, bring this action against Defendants FibroGen, Inc. ("FibroGen") and AstraZeneca AB ("AstraZeneca") (collectively, "Defendants") to obtain a declaratory judgment that the claims of the following patents are invalid and not infringed: U.S. Patent Nos. 8,318,703 ("'703 patent"), 8,466,172 ("'172 patent), 8,614,204 ("'204 patent"), 9,920,011 ("'011 patent"), 8,629,131 ("'131 patent"), 8,604,012 ("'012 patent"), 8,609,646 ("'646 patent"), 8,604,013 ("'013 patent"), 10,626,090 ("'090 patent"), 10,894,774 ("'774 patent"), 10,882,827 ("'827 patent"), and 10,927,081 ("'081 patent") (collectively, the "patents-in-suit").

NATURE OF THE ACTION

1. Millions of Americans suffer from chronic kidney disease ("CKD"). CKD is a debilitating and often fatal condition characterized by a gradual loss of kidney function over time. This loss of kidney function leads to other health complications in CKD patients. One

common complication is anemia, which is a condition in which a person does not have enough healthy red blood cells.

2. Akebia is a leading innovative pharmaceutical company focused on developing treatments for patients with kidney disease. Akebia has developed the drug vadadustat to treat anemia associated with CKD.

3. Vadadustat is a hypoxia-inducible factor prolyl hydroxylase inhibitor ("HIF-PHI"). Vadadustat works by mimicking the physiological effect of altitude on oxygen availability, which stimulates the production of red blood cells.

4. Akebia has completed Phase 3 clinical trials for vadadustat, which have demonstrated the efficacy and safety of the drug as a treatment for anemia associated with CKD in dialysis patients.

5. On March 29, 2021, Akebia filed a New Drug Application with the U.S. Food and Drug Administration ("FDA"), seeking approval to market vadadustat in the United States for the treatment of anemia associated with CKD in adults on dialysis and not on dialysis. Upon FDA approval, Akebia and Otsuka America will together commercialize vadadustat in the United States, including in this District, for its approved indication(s).

6. The current standard of care for anemia associated with CKD involves the use of injectable medicines or blood transfusions. By contrast, vadadustat is an orally-administered tablet taken once per day. If approved by the FDA, vadadustat will represent a significant advance in patient care and convenience for those suffering from anemia associated with CKD.

7. FibroGen is a pharmaceutical company that is developing a different HIF-PHI called roxadustat. Roxadustat and vadadustat are both orally-administered HIF-PHIs that are being developed as treatments for anemia associated with CKD.

8. Upon information and belief, FibroGen has exclusively licensed certain rights to commercialize roxadustat in the United States to AstraZeneca. Upon information and belief, Defendants have sought FDA approval to market roxadustat in the United States, including in this District, but the FDA has not yet completed its review of that application.

9. FibroGen holds several patents relating to HIF-PHIs. FibroGen's patents include claims to unduly broad methods of using vast genera encompassing countless compounds, in an apparent effort to close the field of HIF-PHIs to competition. Each of FibroGen's patents, however, contains only a limited disclosure of testing for a handful of compounds. Each of FibroGen's patents thus falls far short of describing or enabling the use of all HIF-PHIs or the vast genera for the claimed uses.

10. FibroGen's patents do not describe or enable vadadustat, and FibroGen has no valid patent claim that covers vadadustat or its use. Moreover, during prosecution of certain of its patents, FibroGen has distinguished the use of HIF-PHIs to treat anemia associated with CKD in order to obtain allowance of its patent claims directed to the use of HIF-PHIs to treat anemia of chronic disease.

11. Although FibroGen did not discover or develop vadadustat—and roxadustat has a different chemical structure from vadadustat—FibroGen has sought to use its patents related to HIF-PHIs to stifle competition by vadadustat. For example, the exclusive licensee of FibroGen's patents related to HIF-PHIs in the United Kingdom filed an infringement action against Akebia and Otsuka Pharmaceutical Co., Ltd., in the United Kingdom in 2019 that asserted that the use of vadadustat will infringe the European counterparts to the patents-in-suit. In a decision rendered in April 2020, the United Kingdom's High Court of Justice declared five of six FibroGen patents litigated to judgment invalid and a sixth patent not infringed. Akebia and FibroGen have also

been engaged in legal proceedings in various other jurisdictions around the world relating to FibroGen's patents relating to HIF-PHIs, which have resulted in FibroGen's broad genus claims being declared invalid or in FibroGen making narrowing amendments to its patents. FibroGen has focused its recent patent prosecution on obtaining patents that purport to be directed to the treatment of anemia associated with CKD, confirming FibroGen's intent to use its patents to try to stifle competition in this area. Indeed, certain claims of FibroGen's recently issued patents do not even cover roxadustat, which confirms FibroGen's strategy to extend its patent rights far beyond anything that FibroGen can purport to have invented.

12. Upon information and belief, AstraZeneca is the exclusive licensee of FibroGen's patents relating to HIF-PHIs in the United States. Upon information and belief, AstraZeneca has rights to assert FibroGen's patents relating to HIF-PHIs against alleged third party infringement in the United States pursuant to the publicly available redacted version of AstraZeneca's license agreement with FibroGen, which is on file with the SEC.

13. Given the history of litigation between the parties, and given FibroGen's recent patent prosecution strategy aimed at stifling competition in connection with treatments for anemia associated with CKD, Plaintiffs reasonably believe that upon or before FDA's approval of vadadustat, Defendants will assert FibroGen's patents in an effort to obstruct Plaintiffs' marketing and sale of vadadustat in the United States. Plaintiffs bring this action for a declaratory judgment of patent invalidity and noninfringement now, so that Defendants may not interfere or disrupt with baseless claims of patent infringement the marketing and sale of vadadustat in the United States upon FDA approval. Through this action, Plaintiffs seek to confirm in the United States what other jurisdictions around the world have already found—that

the broad, generic patent claims that FibroGen has obtained are not a valid basis for Defendants to stifle competition from Plaintiffs' planned marketing of vadadustat.

PARTIES

14. Plaintiff Akebia is a Delaware corporation with its principal place of business at 245 First Street, Cambridge, MA 02142.

15. Plaintiff Otsuka America is a Delaware corporation with its principal place of business at 508 Carnegie Center Drive, Princeton, NJ 08540.

16. Upon information and belief, Defendant FibroGen is a Delaware corporation with its principal place of business at 409 Illinois Street, San Francisco, CA 94158.

17. Upon information and belief, Defendant AstraZeneca is a Swedish corporation with a place of business at Karlebyhus, Astraallén, Södertälje, S-151 85, Sweden.

JURISDICTION AND VENUE

18. This Court has personal jurisdiction over FibroGen because, among other things, it is a Delaware corporation.

19. This Court has personal jurisdiction over AstraZeneca by virtue of its contacts with this District, including specific contacts with this District that give rise to this civil action. For example, AstraZeneca regularly conducts business in the State of Delaware through its corporate affiliates, including AstraZeneca Pharmaceuticals LP, which is a Delaware corporation with a principal place of business at 1800 Concord Pike, Wilmington, DE 19803. Furthermore, upon information and belief, AstraZeneca has purposefully directed conduct towards this District by entering into its exclusive license agreement with FibroGen, a Delaware corporation, to commercialize roxadustat in the United States, including in this District. Upon information and belief, this license agreement grants to AstraZeneca rights to sue third parties for alleged

infringement of the patents-in-suit, including in connection with vadadustat, and necessitates ongoing contact with this District by requiring cooperation with FibroGen, a Delaware corporation, in any patent enforcement litigation brought by FibroGen or AstraZeneca. AstraZeneca also has purposefully and repeatedly availed itself of the benefits and protections of the courts in Delaware, including as a frequent plaintiff enforcing patents by bringing multiple patent infringement actions before this Court. *See, e.g.*, *AstraZeneca AB v. Alembic Pharm. Ltd.*, C.A. No. 20-202-RGA (D. Del.); *AstraZeneca AB v. Aurobindo Pharma USA Inc.*, C.A. No. 19-2113-RGA (D. Del.); *AstraZeneca AB v. MSN Pharm., Inc.*, C.A. No. 18-2051-RGA (D. Del.); *AstraZeneca AB v. Apotex Inc.*, C.A. No. 18-2010-RGA (D. Del.); *AstraZeneca AB v. Teva Pharm. USA, Inc.*, C.A. No. 18-1685-CFC (D. Del.); *AstraZeneca AB v. Mylan Pharm. Inc.*, C.A. No. 18-1562-CFC (D. Del.); *AstraZeneca AB v. Hisun Pharm. Co.*, C.A. No. 18-1232-RGA (D. Del.); *AstraZeneca AB v. Zydus Pharm. (USA) Inc.*, C.A. No. 18-664-RGA (D. Del.); and *AstraZeneca AB v. Fresenius Kabi USA, LLC*, C.A. No. 17-1795-VAC (D. Del.).

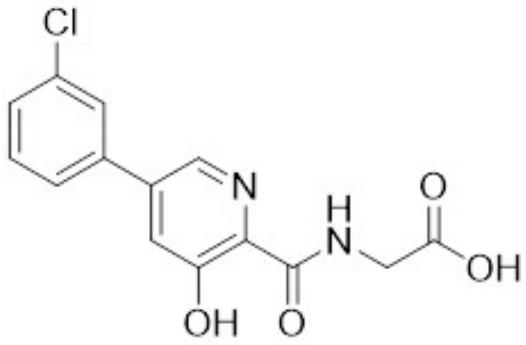
20. This is a declaratory judgment action arising under 28 U.S.C. §§ 2201 and 2202 and the patent laws of the United States, codified in title 35 of the United States Code. This Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. §§ 1331 and 1338(a). An actual, substantial, and continuing justiciable controversy exists based upon Plaintiffs' plans to market vadadustat in the United States upon FDA approval and FibroGen's history of asserting its patents relating to HIF-PHIs against vadadustat outside of the United States. In addition, FibroGen's recent patent prosecution strategy has focused on obtaining claims that purport to cover the treatment of anemia associated with CKD, the same indication being sought for vadadustat at the FDA. Plaintiffs reasonably believe that, like they have in countries around

the world, Defendants will assert that the marketing of vadadustat in the United States infringes FibroGen's patents relating to HIF-PHIs.

21. Venue is proper in this judicial district under 28 U.S.C. § 1391 because, among other things, FibroGen is a Delaware corporation and AstraZeneca is subject to this Court's personal jurisdiction in this action.

VADADUSTAT

22. Vadadustat is a compound with the chemical name 2-[[5-(3-chlorophenyl)-3-hydroxypyridine-2-carbonyl]amino]acetic acid. Vadadustat has the following chemical structure:



23. Akebia has obtained patents in the United States claiming vadadustat and its use, including but not limited to U.S. Patent Nos. 7,811,595, 8,323,671, 8,343,952, 8,598,210, 8,940,773, 9,701,636, RE47,437, 9,987,262, and 10,149,842.

24. Akebia filed an Investigational New Drug Application for vadadustat with the FDA in 2009 and began clinical development of vadadustat. Akebia has conducted several clinical trials of vadadustat to assess it as a treatment for anemia associated with CKD. In 2020, Akebia announced the results of its Phase 3 clinical trials that evaluated the use of vadadustat to treat anemia associated with CKD. Akebia's Phase 3 clinical trials showed that vadadustat is safe and effective in treating anemia associated with CKD in dialysis patients.

25. On March 29, 2021, Akebia submitted a New Drug Application to the FDA seeking approval to market vadadustat in the United States for the treatment of anemia associated with CKD in adults on dialysis and not on dialysis. Akebia's application has been assigned NDA No. 215192. Upon FDA approval, Akebia and Otsuka America intend to market vadadustat in the United States, including in this District, for its approved indication(s) under the brand name Vafseo™.

26. The current standard of care for treatment of anemia associated with CKD are injectable drugs, such as Epogen® (epoetin alfa) and Aranesp® (darbepoetin alfa), or blood transfusion. Unlike those existing therapies, vadadustat is administered orally as a tablet that patients can take once daily. Vadadustat has the potential to greatly improve patient care and convenience by treating anemia associated with CKD with an orally administered tablet.

FIBROGEN'S PATENTS

27. FibroGen has aggressively pursued patent claims purporting to cover the use of a vast number of purported HIF-PHI compounds that it never made or tested to treat various types of anemia and other conditions. Upon information and belief, Defendants intend to assert these invalid and not infringed patent claims against Plaintiffs and their vadadustat product in an attempt to obstruct U.S. competition to its HIF-PHI product, roxadustat.

28. U.S. Patent No. 8,318,703 is titled "Methods for Improving Kidney Function." The '703 patent issued on November 27, 2012. Upon information and belief, FibroGen is the owner by assignment of the '703 patent. A copy of the '703 patent is attached hereto as Exhibit A.

29. U.S. Patent No. 8,466,172 is titled "Stabilization of Hypoxia Inducible Factor (HIF) Alpha." The '172 patent issued on June 18, 2013. Upon information and belief, FibroGen

is the owner by assignment of the '172 patent. A copy of the '172 patent is attached hereto as Exhibit B.

30. U.S. Patent No. 8,614,204 is titled "Enhanced Erythropoiesis and Iron Metabolism." The '204 patent issued on December 24, 2013. Upon information and belief, FibroGen is the owner by assignment of the '204 patent. A copy of the '204 patent is attached hereto as Exhibit C.

31. U.S. Patent No. 9,920,011 is titled "Enhanced Erythropoiesis and Iron Metabolism." The '011 patent issued on March 20, 2018. Upon information and belief, FibroGen is the owner by assignment of the '011 patent. A copy of the '011 patent is attached hereto as Exhibit D.

32. U.S. Patent No. 8,629,131 is titled "Enhanced Erythropoiesis and Iron Metabolism." The '131 patent issued on January 14, 2014. Upon information and belief, FibroGen is the owner by assignment of the '131 patent. A copy of the '131 patent is attached hereto as Exhibit E.

33. U.S. Patent No. 8,604,012 is titled "Enhanced Erythropoiesis and Iron Metabolism." The '012 patent issued on December 10, 2013. Upon information and belief, FibroGen is the owner by assignment of the '012 patent. A copy of the '012 patent is attached hereto as Exhibit F.

34. U.S. Patent No. 8,609,646 is titled "Enhanced Erythropoiesis and Iron Metabolism." The '646 patent issued on December 17, 2013. Upon information and belief, FibroGen is the owner by assignment of the '646 patent. A copy of the '646 patent is attached hereto as Exhibit G.

35. U.S. Patent No. 8,604,013 is titled "Enhanced Erythropoiesis and Iron Metabolism." The '013 patent issued on December 10, 2013. Upon information and belief, FibroGen is the owner by assignment of the '013 patent. A copy of the '013 patent is attached hereto as Exhibit H.

36. U.S. Patent No. 10,626,090 is titled "Enhanced Erythropoiesis and Iron Metabolism." The '090 patent issued on April 21, 2020. Upon information and belief, FibroGen is the owner by assignment of the '090 patent. A copy of the '090 patent is attached hereto as Exhibit I.

37. U.S. Patent No. 10,894,774 is titled "Enhanced Erythropoiesis and Iron Metabolism." The '774 patent issued on January 19, 2021. Upon information and belief, FibroGen is the owner by assignment of the '774 patent. A copy of the '774 patent is attached hereto as Exhibit J.

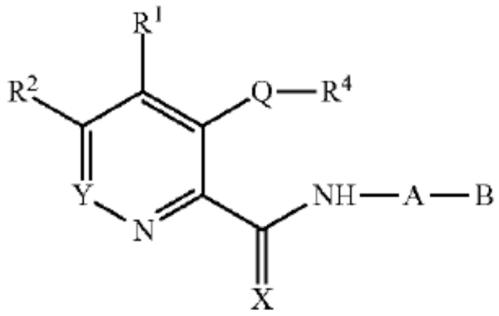
38. U.S. Patent No. 10,882,827 is titled "Enhanced Erythropoiesis and Iron Metabolism." The '827 patent issued on January 5, 2021. Upon information and belief, FibroGen is the owner by assignment of the '827 patent. A copy of the '827 patent is attached hereto as Exhibit K.

39. U.S. Patent No. 10,927,081 is titled "Enhanced Erythropoiesis and Iron Metabolism." The '081 patent issued on February 23, 2021. Upon information and belief, FibroGen is the owner by assignment of the '081 patent. A copy of the '081 patent is attached hereto as Exhibit L.

40. Upon information and belief, AstraZeneca is the exclusive licensee of the patents-in-suit. Upon information and belief, AstraZeneca has rights to assert the patents-in-suit against alleged infringement by third parties pursuant to its license agreement with FibroGen. Upon

information and belief, FibroGen also has rights to assert the patents-in-suit against alleged infringement by third parties.

41. The claims of the patents-in-suit purport to encompass vast numbers of compounds that, upon information and belief, have never been made, let alone shown to have properties suitable for treatment of patients with the claimed conditions. For example, the claims of the ’090 patent recite a chemical genus of compounds with the following generic chemical structure:



The list of potential chemical groups that may be incorporated within that generic chemical structure spans 10 columns of text in the patent. *See* ’090 patent, columns 63-72. The number of compounds encompassed by that generic structure is for all practical purposes unlimited. In fact, the claimed genus encompasses on the order of at least 10^{183} compounds. *Akebia Therapeutics, Inc. v. FibroGen, Inc.*, [2020] EWHC 866 (Pat), ¶ 368 (Apr. 20, 2020). This number is so large that it is more than a million times larger than the estimated number of grains of sand on all of the beaches on Earth. In addition to the ’090 patent, this genus is also recited in claims 1-9 of the ’774 patent and in claim 6 of the ’011 patent.

42. The claims of the ’703, ’172, ’204, ’646, ’012, ’013, and ’131 patents, and claims 1-5 of the ’011 patent, are even broader and are directed to “an agent” or “a heterocyclic carboxamide compound” without imposing any further limitations on the compound’s structure.

43. Notwithstanding these claims purporting to cover a vast number of compounds for the treatment of certain forms of anemia and other conditions, the specifications of the patents-in-suit describe only a handful of exemplary compounds. Across all of the patents-in-suit, the specifications exemplify and provide testing data for no more than 20 compounds. There is absolutely no indication in the specifications to show that the inventors were in possession of the full scope of their claimed chemical genera. Moreover, the specifications of the patents-in-suit provide insufficient guidance to permit a person of ordinary skill in the art to select compounds to achieve the claimed functions without undue experimentation. Upon information and belief, numerous compounds within the claimed chemical genera do not work for their claimed method of treatment. Upon information and belief, FibroGen is already aware that numerous compounds within the claimed chemical genera do not work for their claimed method of treatment.

44. None of the patents-in-suit discloses the chemical structure for vadadustat. Similarly, none of the patents-in-suit discloses any testing or other data for vadadustat.

45. As information about vadadustat and its successful clinical trials has become public, and as FibroGen's patent claims to broad genera of compounds have been declared invalid in jurisdictions around the world, FibroGen, upon information and belief, has endeavored to obtain additional patent claims to assert against Plaintiffs.

46. For example, in August 2020, FibroGen for the first time sought patent claims directed to two narrower chemical genera, as compared with FibroGen's earlier patents. *See, e.g.*, '081 patent, claims 1-46; '827 patent, claims 1-24; '774 patent, claim 10-23. These narrower chemical genera are not described in the originally filed specifications for any of FibroGen's patents. The first time that these narrower chemical genera were included in any of

FibroGen's patents or patent prosecution efforts was through an amendment to the claims that FibroGen proposed during prosecution on August 21, 2020. *See* File History for U.S. Patent Appl. No., 15/498,856, Supplemental Response (Aug. 21, 2020). The chemical genera recited in claims 10-23 of the '774 patent, claims 1-24 of the '827 patent, and claims 1-46 of the '081 patent do not even cover roxadustat, which confirms FibroGen's strategy to extend its patent rights beyond anything that it can purport to have invented.

47. To the extent that Defendants assert that these narrower chemical genera are entitled to a priority date earlier than August 21, 2020, claims containing those genera are invalid for, *inter alia*, lack of written description and enablement. To the extent that Defendants assert that claims reciting these narrower chemical genera encompass vadadustat and its uses, those claims are invalid for, *inter alia,* anticipation and/or obviousness in view of the numerous publications disclosing vadadustat and its uses prior to August 21, 2020.

48. Upon information and belief, discovery in this action will show that, at the time of filing any of the applications that led to the patents-in-suit, none of the named inventors of those patents had any documentation of the narrower chemical genera recited in claims 1-46 of the '081 patent, claims 1-24 of the '827 patent, or claims 10-23 of the '774 patent.

49. In any event, even these "narrower" claims still include a vast number of compounds, and the specifications for the '081, '827, and '774 patents do not provide adequate written description for the full scope of the claimed chemical genera. Nor do the specifications of these patents provide sufficient guidance to enable a person of ordinary skill in the art to select compounds to achieve the claimed functions without undue experimentation.

50. In addition, in order to obtain and defend the validity of its overly broad patent claims, FibroGen has repeatedly distinguished the claimed methods of treatment from the

treatment of anemia associated with CKD. For example, during prosecution of the '204 patent, FibroGen distinguished its claimed methods of treating anemia of chronic disease and of increasing serum iron from the treatment of anemia associated with CKD. *See* File History for U.S. Patent Appl. No., 10/861,590, Response to Office Action at 15-17 (Sept. 25, 2009). In opposition proceedings before the European Patent Office relating to counterparts to the patents-in-suit, FibroGen has similarly distinguished its claimed methods of treating anemia of chronic disease from the treatment of anemia associated with CKD. *See, e.g.*, FibroGen's Grounds of Appeal for EP2,322,155, at 4 (Nov. 28, 2017). Despite those prior statements distinguishing the treatment of anemia associated with CKD, FibroGen has nevertheless recently reversed course and obtained patent claims in the United States that purport to cover the use of HIF-PHIs to treat anemia associated with CKD. *See* '081 patent, claims 1-24 (reciting methods of treating anemia in a human subject with kidney disease) and claims 25-46 (reciting methods of treating anemia in a human subject with chronic renal failure).

PROCEEDINGS RELATING TO FIBROGEN'S PATENTS

51. For the past several years, the parties have litigated the invalidity and noninfringement of foreign counterparts to the patents-in-suit in jurisdictions throughout the world. Those proceedings have repeatedly confirmed the invalidity of FibroGen's broad, generic patent claims, such as those at issue in this case.

52. For example, on December 5, 2013, Akebia filed an opposition in the European Patent Office ("EPO") against FibroGen's European Patent No. 1463823 ("EP '823 patent"), which is related to the '703 and '172 patents at issue in this case. Following the oral proceeding, the Opposition Division of EPO ruled that the patent as granted did not meet the sufficiency requirement for patentability under the European Patent Convention (which is analogous to

certain of the requirements under 35 U.S.C. § 112) and, therefore, revoked the patent in its entirety.

53. On June 2, 2014, Akebia filed an invalidity proceeding before the Japan Patent Office ("JPO") against certain claims of FibroGen's Japanese Patent No. 4804131 ("JP '131 patent"), which is related to the '703 and '172 patents at issue in this case. The JPO issued a preliminary decision finding all the challenged claims to be invalid for lack of an inventive step (which is analogous to the requirements under 35 U.S.C. § 103). FibroGen subsequently amended the claims, and the JPO accepted the amendments. The amended JP '131 patent does not cover vadadustat or any pyridine carboxamide compounds.

54. Between May and July 2015, Akebia filed oppositions to FibroGen's European Patent Nos. 2322155 ("EP '155 patent"), 1633333 ("EP '333 patent"), and 2322153 ("EP '153 patent") in the EPO, requesting the patents be revoked in their entirety. These patents are related to the '204, '011, '131, '012, '646, '013, '090, '774, '827, and '081 patents at issue in this case. Following an oral hearing, the EPO ruled that the EP '333 patent's claims lack novelty (which is analogous to the requirements under 35 U.S.C. § 102) and the EP '155 patent's claims lack novelty and inventive step (which is analogous to the requirements under 35 U.S.C. §§ 102 and 103) and, therefore, revoked the patents in their entirety. The Opposition Division of the EPO maintained the EP '153 patent after FibroGen significantly narrowed the claims to a compound for use in increasing serum iron in treating iron deficiency in a subject, an indication for which vadadustat is not intended to be developed.

55. On May 21, 2018, Akebia filed a Statement of Claim in Canadian Federal Court to challenge the validity of three of FibroGen's patents related to HIF-PHIs in Canada: CA 2467689, CA 2468083, and CA 2526496. CA 2467689 and CA 2468083 are related to the '703

and ’172 patents at issue in the case, while CA 2526496 is related to the ’204, ’011, ’131, ’012, ’646, ’013, ’090, ’774, ’827, and ’081 patents at issue in this case. On June 25, 2020, the parties agreed to dismiss the CA 2467689 patent from the lawsuit. On February 16, 2021, the parties agreed to dismiss the lawsuit in its entirety.

56. On December 13, 2018, Akebia and Otsuka Pharmaceutical Co., Ltd., filed a lawsuit challenging the validity of FibroGen’s six patents related to HIF-PHIs in the United Kingdom: the EP ’823 patent, the EP ’333 patent, the EP ’153 patent, the EP ’155 patent, European Patent No. 2289531 (“the EP ’531 patent”), and European Patent No. 2298301 (“the EP ’301 patent”). The EP ’823 patent, the EP ’531 patent, and the EP ’301 patent are related to the ’703 and ’172 patents at issue in this case, while the EP ’333 patent, the EP ’531 patent, and the EP ’301 patent are related to the ’204, ’011, ’131, ’012, ’646, ’013, ’090, ’774, ’827, and ’081 patents at issue in this case. In May 2019, the exclusive licensee of FibroGen’s patents in the United Kingdom sued Akebia and Otsuka Pharmaceutical Co., Ltd., for infringement of those six patents in the United Kingdom. Following trial, the court issued a judgment in favor of Akebia and Otsuka Pharmaceutical Co., Ltd. The court’s judgment invalidated all the claims at issue in each of the EP ’823 patent, the EP ’333 patent, the EP ’153 patent, the EP ’155 patent, and the EP ’301 patent for insufficient disclosure. The EP ’531 patent was amended to a single claim to recite one specific compound; this claim was held to be valid but not infringed by vadadustat.

57. These proceedings around the world regarding Defendants’ patents and Plaintiffs’ vadadustat product show that there is an actual, justiciable, and continuing controversy between Defendants and Plaintiffs with respect to Defendants’ patents and Plaintiffs’ vadadustat product that is amenable to resolution by this Court at this time. By granting the relief sought by

Plaintiffs, the Court would prevent an imminent injury: obstruction of the launch and sale of Plaintiffs' vadadustat product in the United States caused by Defendants' assertion of patents that are invalid and not infringed by Plaintiffs' vadadustat product. The controversy between Plaintiffs and Defendants is of sufficient immediacy and reality to warrant the exercise of this Court's jurisdiction, as confirmed by the fact that multiple courts and patent offices around the world have been able to address and resolve this controversy on the current record.

COUNT I

(Declaratory Judgment of Invalidity of U.S. Patent No. 8,318,703)

58. Plaintiffs repeat and reallege Paragraphs 1-57 of this Complaint.

59. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding the validity of the '703 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '703 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '703 patent. Upon information and belief, Defendants contend that the claims of the '703 patent are valid.

60. The '172 and '703 patents belong to the same patent family, and both claim priority, either directly or indirectly, to U.S. Application No. 10/313,551, now abandoned.

61. Claims 1 and 8 are the only independent claims of the '703 patent. Independent claim 1 of the '703 patent recites a "method for improving kidney function in a subject having impaired kidney function, the method comprising administering to the subject an effective amount of an agent that inhibits hypoxia inducible factor (HIF) hydroxylase activity." Independent claim 8 of the '703 patent recites a "method for increasing glomerular filtration rate

(GFR) in a subject having a decreased GFR, the method comprising administering to the subject an effective amount of an agent that inhibits HIF hydroxylase activity."

62. The claims of the '703 patent are invalid for failure to comply with one or more of the conditions of patentability under Title 35 of the United States Code and related judicial doctrines, including but not limited to 35 U.S.C. §§ 101, 102, 103, and/or 112 and/or obviousness-type double patenting.

63. For example, the claims of the '703 patent are invalid under 35 U.S.C. § 112 because the patent specification fails to provide a written description that conveys with reasonable clarity to a person of ordinary skill in the art that, as of its effective filing date, the purported inventors of the '703 patent were in possession of the subject matter claimed therein. The claims of the '703 patent are also invalid under 35 U.S.C. § 112 because the specification fails to provide an enabling disclosure that teaches a person of ordinary skill in the art how to make and use the full scope of the claimed subject matter without undue experimentation.

64. The specification of the '703 patent discloses biological data for at most 5 compounds. '703 Patent, Examples 1-7. In stark contrast, generic Formula I disclosed by the '703 patent encompasses a "staggeringly large" number of compounds—on the order of at least 10^{183}—and is merely an alleged example of the claimed "agent that inhibits HIF hydroxylase activity." *Akebia Therapeutics, Inc. v. FibroGen, Inc.*, [2020] EWHC 866 (Pat), ¶ 368 (Apr. 20, 2020). There is no teaching or guidance within the specification with regard to which of these 10^{183} molecules referenced in the specification, beyond the 5 allegedly exemplary compounds, have the claimed functional property of "inhibit[ing] HIF hydroxylase activity," "improving kidney function in a subject having impaired kidney function," or "increasing glomerular filtration rate (GFR) in a subject having a decreased GFR."

65. The claimed genus of "an agent" has no structural limitation at all. The compounds of Formula I are merely possible examples of the claimed "agent." The specification thus does not provide sufficient written description to describe or enable the full scope of the claimed genus or even a portion of the genus, i.e., which of the vast number of molecules within the genus of "agent" (or even the compounds of Formula I) is capable of achieving the claimed function of "inhibit[ing] HIF hydroxylase activity," "improving kidney function in a subject having impaired kidney function," or "increasing glomerular filtration rate (GFR) in a subject having a decreased GFR," especially given the unpredictability of the pharmaceutical field. In addition, at the effective filing date of the '703 patent, a person of ordinary skill in the art would have been required to engage in undue experimentation to determine which of the vast number of molecules could achieve the claimed functions, given the unpredictability of the pharmaceutical field.

66. Thus, the specification fails to demonstrate that the applicant possessed or enabled the full scope of the claims to the wholly functionally-defined genus.

67. To the extent that Defendants assert that the claims of the '703 patent are supported by the specification, the claims would have been anticipated under 35 U.S.C. § 102 and/or obvious under 35 U.S.C. § 103 because the broad, functionally claimed genus of HIF-PHIs was known and/or obvious in view of the prior art, which includes, but is not limited to, US 6,093,730; Ivan et al., Science, 292, 464-468, 2001; Jaakkola et al., Science, 292, 468-472, 2001; Ivan et al., PNAS, Vol. 99, 13459-13464, 2002; Epstein et al., Cell, Vol. 107, 43-54, October 5, 2001; WO2001/064652; WO2003/053997; and WO2003/049686.

68. Plaintiffs therefore are entitled to a judicial declaration that the claims of the '703 patent are invalid.

COUNT II

(Declaratory Judgment of Noninfringement of U.S. Patent No. 8,318,703)

69. Plaintiffs repeat and reallege Paragraphs 1-68 of this Complaint.

70. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding infringement of the '703 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '703 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '703 patent.

71. Plaintiffs' manufacture, use, sale, offer for sale, or importation of vadadustat has not infringed and will not infringe, either directly or indirectly, any valid claim of the '703 patent, either literally or under the doctrine of equivalents.

72. For example, claims 1 and 8 are the only independent claims of the '703 patent. Independent claim 1 of the '703 patent is directed to a "method for improving kidney function" and independent claim 8 of the '703 patent is directed to a "method for increasing glomerular filtration rate." Akebia is not seeking FDA approval for vadadustat for any indication to improve kidney function or increase glomerular filtration rate. The use of vadadustat in accordance with its proposed label therefore will not infringe any claim of the '703 patent, and Plaintiffs' marketing of vadadustat for use in accordance with its proposed label will not induce or contribute to infringement of any claim of the '703 patent.

73. In addition, the specification for the '703 patent does not disclose the structure of vadadustat or any data for vadadustat. There is no disclosure in the '703 patent that would have led a person of ordinary skill in the art to use vadadustat to practice the claimed methods. To the

extent that Defendants assert that the claims of the '703 patent nevertheless encompass the use of vadadustat, the claims of the '703 patent would be invalid for lack of adequate written description and lack of enablement under 35 U.S.C. § 112.

74. Finally, for at least the reasons described above in Count I, the claims of the '703 patent are invalid. Plaintiffs cannot be held liable for infringement of invalid patent claims.

75. Plaintiffs are therefore entitled to a judicial declaration that their making, using, selling, offering to sell, or importing vadadustat has not infringed and will not infringe any valid claim of the '703 patent.

COUNT III

(Declaratory Judgment of Invalidity of U.S. Patent No. 8,466,172)

76. Plaintiffs repeat and reallege Paragraphs 1-75 of this Complaint.

77. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding the validity of the '172 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '172 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '172 patent. Upon information and belief, Defendants contend that the claims of the '172 patent are valid.

78. The '172 and '703 patents belong to the same patent family, and both claim priority, either directly or indirectly, to U.S. Application No. 10/313,551, now abandoned.

79. Claim 1 is the only independent claim in the '172 patent. Independent claim 1 of the '172 patent recites a "method for treating a hypoxic or ischemic disorder or condition in a

subject, the method comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia inducible factor (HIFα)."

80. The claims of the '172 patent are invalid for failure to comply with one or more of the conditions of patentability under Title 35 of the United States Code and related judicial doctrines, including but not limited to 35 U.S.C. §§ 101, 102, 103, and/or 112 and/or obviousness-type double patenting.

81. For example, the claims of the '172 patent are invalid under 35 U.S.C. § 112 because the patent specification fails to provide a written description that conveys with reasonable clarity to a person of ordinary skill in the art that, as of its effective filing date, the purported inventors of the '172 patent were in possession of the subject matter claimed therein. The claims of the '172 patent are also invalid under 35 U.S.C. § 112 because the specification fails to provide an enabling disclosure that teaches a person of ordinary skill in the art how to make and use the full scope of the claimed subject matter without undue experimentation.

82. The specification of the '172 patent discloses *in vivo* data for at most 5 compounds and *in vitro* data for at most 17 compounds. '172 Patent, Examples 1, 2, 3, 5, 6, 7, 8, 9. In stark contrast, generic Formula I disclosed by the '172 patent encompasses a "staggeringly large" number of compounds—on the order of at least 10^{183}—and is merely an alleged example of the claimed "heterocyclic carboxamide compound." *Akebia Therapeutics, Inc. v. FibroGen, Inc.*, [2020] EWHC 866 (Pat), ¶ 368 (Apr. 20, 2020). There is no teaching or guidance within the specification with regard to which of these 10^{183} molecules referenced in the specification, beyond the 17 allegedly exemplary compounds, have the claimed functional property of "treating a hypoxic or ischemic disorder or condition in a subject" or "stabiliz[ing] the alpha subunit of hypoxia inducible factor (HIFα)."

83. The claimed structural genus of "a heterocyclic carboxamide compound" encompasses a vast number of compounds. The specification does not provide sufficient written description to identify which compounds within the vast structural genus of "a heterocyclic carboxamide compound" is capable of achieving the claimed function of "treating a hypoxic or ischemic disorder or condition in a subject" or "stabiliz[ing] the alpha subunit of hypoxia inducible factor (HIFα)," especially given the unpredictability of the pharmaceutical field. In addition, at the effective filing date of the '172 patent, a person of ordinary skill in the art would have been required to engage in undue experimentation to determine which of the vast number of compounds within the structural genus of "a heterocyclic carboxamide compound" could achieve the claimed functions, given the unpredictability of the pharmaceutical field.

84. Thus, the specification fails to demonstrate that the applicant possessed or enabled the full scope of the claims to the functionally-defined genus.

85. To the extent that Defendants assert that the claims of the '172 patent are supported by the specification, the claims would have been anticipated under 35 U.S.C. § 102 and/or obvious under 35 U.S.C. § 103 because the broad, functionally claimed genus of HIF-PHIs was known and/or obvious in view of the prior art, which includes, but is not limited to, U.S. Patent No. 6,093,730; WO2001/064652; Ivan et al., Science, 292, 464-468, 2001; Jaakkola et al., Science, 292, 468-472, 2001; Ivan et al., PNAS, Vol. 99, 13459-13464, 2002; and Epstein et al., Cell, Vol. 107, 43-54, October 5, 2001.

86. Plaintiffs therefore are entitled to a judicial declaration that the claims of the '172 patent are invalid.

COUNT IV

(Declaratory Judgment of Noninfringement of U.S. Patent No. 8,466,172)

87. Plaintiffs repeat and reallege Paragraphs 1-86 of this Complaint.

88. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding infringement of the '172 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '172 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '172 patent.

89. Plaintiffs' manufacture, use, sale, offer for sale, or importation of vadadustat has not infringed and will not infringe, either directly or indirectly, any valid claim of the '172 patent, either literally or under the doctrine of equivalents.

90. For example, claim 1 is the only independent claim in the '172 patent. Claim 1 recites a "method for treating a hypoxic or ischemic disorder or condition." The use of vadadustat in accordance with its proposed label will not infringe any valid claim of the '172 patent, and Plaintiffs' marketing of vadadustat for use in accordance with its proposed label will not induce or contribute to infringement of any valid claim of the '172 patent.

91. In addition, the specification for the '172 patent does not disclose the structure of vadadustat or any data for vadadustat. There is no disclosure in the '172 patent that would have led a person of ordinary skill in the art to use vadadustat to practice the claimed methods. To the extent that Defendants assert that the claims of the '172 patent nevertheless encompass the use of vadadustat, the claims of the '172 patent would be invalid for lack of adequate written description and lack of enablement under 35 U.S.C. § 112.

92. Finally, for at least the reasons described above in Count III, the claims of the '172 patent are invalid. Plaintiffs cannot be held liable for infringement of invalid patent claims.

93. Plaintiffs are therefore entitled to a judicial declaration that their making, using, selling, offering to sell, or importing vadadustat has not infringed and will not infringe any valid claim of the '172 patent.

COUNT V

(Declaratory Judgment of Invalidity of U.S. Patent No. 8,614,204)

94. Plaintiffs repeat and reallege Paragraphs 1-93 of this Complaint.

95. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding the validity of the '204 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '204 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '204 patent. Upon information and belief, Defendants contend that the claims of the '204 patent are valid

96. The '204, '011, '131, '012, '646, '013, and '090 patents belong to the same patent family, and the '011, '131, '012, '646, '013, and '090 patents all claim priority, either directly or indirectly, to the '204 patent.

97. Claims 1, 4, and 6 are the only independent claims of the '204 patent. Independent claim 1 of the '204 patent recites a "method for treating iron deficiency in a subject in need thereof, the method comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia inducible factor

(HIFα), thereby treating iron deficiency in the subject." Independent claim 4 of the '204 patent recites a "method for treating functional iron deficiency in a subject in need thereof, the method comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia inducible factor (HIFα), thereby treating functional iron deficiency in the subject." Independent claim 6 of the '204 patent recites a "method for treating anemia of chronic disease in a subject in need thereof, the method comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia inducible factor (HIFα), thereby treating anemia of chronic disease in the subject."

98. The claims of the '204 patent are invalid for failure to comply with one or more of the conditions of patentability under Title 35 of the United States Code and related judicial doctrines, including but not limited to 35 U.S.C. §§ 101, 102, 103, and/or 112 and/or obviousness-type double patenting.

99. For example, the claims of the '204 patent are invalid under 35 U.S.C. § 112 because the patent specification fails to provide a written description that conveys with reasonable clarity to a person of ordinary skill in the art that, as of its effective filing date, the purported inventors of the '204 patent were in possession of the subject matter claimed therein. The claims of the '204 patent are also invalid under 35 U.S.C. § 112 because the specification fails to provide an enabling disclosure that teaches a person of ordinary skill in the art how to make and use the full scope of the claimed subject matter without undue experimentation. At least claims 9, 11, and 13 of the '204 patent are also indefinite for failing to particularly point out and distinctly claim the subject matter of the alleged invention.

100. The specification of the '204 patent merely provides biological testing data for at most 4 exemplary compounds, Compounds A-D. '204 patent, 15:7-17. In stark contrast, generic Formula I disclosed by the '204 patent encompasses a "staggeringly large" number of compounds—on the order of at least 10^{183}—and is merely an alleged example of the claimed "heterocyclic carboxamide compound." *Akebia Therapeutics, Inc. v. FibroGen, Inc.*, [2020] EWHC 866 (Pat), ¶ 368 (Apr. 20, 2020). There is no teaching or guidance within the specification with regard to which of these 10^{183} molecules referenced in the specification, beyond the 4 allegedly exemplary compounds, have the claimed functional property of "treating iron deficiency," "treating functional iron deficiency," "treating anemia of chronic disease," or "stabiliz[ing] the alpha subunit of hypoxia inducible factor (HIFα)."

101. The claimed structural genus of "a heterocyclic carboxamide compound" encompasses a vast number of compounds. The specification does not provide sufficient written description to support that such a vast number of compounds within the genus of "a heterocyclic carboxamide compound" are capable of achieving the claimed function of "treating iron deficiency," "treating functional iron deficiency," "treating anemia of chronic disease," or "stabiliz[ing] the alpha subunit of hypoxia inducible factor (HIFα)," especially given the unpredictability of the pharmaceutical field. In addition, at the effective filing date of the '204 patent, a person of ordinary skill in the art would have been required to engage in undue experimentation to determine which of the vast number of compounds within the structural genus of "a heterocyclic carboxamide compound" could achieve the claimed functions, given the unpredictability of the pharmaceutical field.

102. Thus, the specification fails to demonstrate that the applicant possessed or enabled the full scope of the claims to the functionally-defined genus.

103. Additionally, dependent claims 9, 11, and 13 of the '204 patent recite "a structural mimetic of 2-oxoglutarate," for which the specification provides no structural definition, merely stating that such compounds optionally "may inhibit the target 2-oxoglutarate dioxygenase enzyme family member competitively with respect to 2-oxoglutarate and noncompetitively with respect to iron." '204 patent, 27:27-29. Thus, these claims are indefinite because a person of ordinary skill in the art would not be able to understand the bounds of that limitation with reasonable certainty.

104. To the extent that Defendants assert that the claims of the '204 patent are supported by the specification, the claims would have been anticipated under 35 U.S.C. § 102 and/or obvious under 35 U.S.C. § 103 because the broad, functionally claimed genus of HIF-PHIs was known and/or obvious in view of the prior art, which includes, but is not limited to, WO 2002/074981; Ivan et al., Science, 292, 464-468, 2001; Ivan et al., PNAS, Vol. 99, 13459-13464, 2002; Epstein et al., Cell, Vol. 107, 43-54, October 5, 2001; WO2003/053997; and Wiesener et al., Ann. Med. 2003, 35, 183-190.

105. In addition, the '204 patent is also invalid because it claims subject matter that is obvious in light of claims of FibroGen's patents that expire earlier. For example, the '204 patent will expire on June 15, 2026, and the '172 patent will expire on December 6, 2022. The claims of the '204 patent are not patentably distinct from the claims of the '172 patent. For example, claims 1-5 of the '204 patent recite methods "for treating iron deficiency" or "for treating functional iron deficiency," "comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia inducible factor (HIFα)." Claim 1 of the '172 patent recites a "method for treating a hypoxic or ischemic disorder or condition in a subject," "comprising administering to the subject an effective amount

of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia inducible factor (HIFα)." The '172 patent further describes that "[t]he ability of the methods of the invention to increase both endogenous erythropoietin and transport and utilization of iron provides specific advantage in oxygen delivery in both normoxic and hypoxic environments." '172 patent, 40:4-7. Thus, claims 1-5 of the '204 patent are obvious in view of claim 1 of the '172 patent.

106. Claims 6-13 of the '204 patent recite methods "for treating anemia of chronic disease in a subject in need thereof," "comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia inducible factor (HIFα), thereby treating anemia of chronic disease in the subject." Claim 1 of the '172 patent recites a "method for treating a hypoxic or ischemic disorder or condition in a subject," "comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia inducible factor (HIFα)." Thus, claims 6-13 of the '204 patent are obvious in view of claim 1 of the '172 patent.

107. Therefore, the claims of the '204 patent are invalid for obviousness-type double patenting in view of claim 1 of the '172 patent.

108. Plaintiffs therefore are entitled to a judicial declaration that the claims of the '204 patent are invalid.

COUNT VI

(Declaratory Judgment of Noninfringement of U.S. Patent No. 8,614,204)

109. Plaintiffs repeat and reallege Paragraphs 1-108 of this Complaint.

110. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding infringement of the '204 patent. Upon obtaining FDA approval, Plaintiffs

intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '204 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States will infringe the '204 patent.

111. Plaintiffs' manufacture, use, sale, offer for sale, or importation of vadadustat has not infringed and will not infringe, either directly or indirectly, any valid claim of the '204 patent, either literally or under the doctrine of equivalents.

112. For example, claims 1, 4, and 6 are the only independent claims in the '204 patent. Claim 1 recites a "method for treating iron deficiency." Claim 4 recites a "method for treating functional iron deficiency." Claim 6 recites a "method for treating anemia of chronic disease." Akebia is not seeking FDA approval for vadadustat for any indication to treat iron deficiency, functional iron deficiency, or anemia of chronic disease. In fact, during prosecution of the '204 patent, FibroGen distinguished the treatment of anemia associated with CKD (i.e., the proposed indication of vadadustat) from the methods of treatment claimed in the '204 patent. *See* File History for U.S. Patent Appl. No., 10/861,590, Response to Office Action at 15-17 (Sept. 25, 2009). The use of vadadustat in accordance with its proposed label therefore will not infringe any claim of the '204 patent, and Plaintiffs' marketing of vadadustat for use in accordance with its proposed label will not induce or contribute to infringement of any claim of the '204 patent.

113. In addition, the specification for the '204 patent does not disclose the structure of vadadustat or any data for vadadustat. There is no disclosure in the '204 patent that would have led a person of ordinary skill in the art to use vadadustat to practice the claimed methods. To the extent that Defendants assert that the claims of the '204 patent nevertheless encompass the use of

vadadustat, the claims of the '204 patent would be invalid for lack of adequate written description and lack of enablement under 35 U.S.C. § 112.

114. Finally, for at least the reasons described above in Count V, the claims of the '204 patent are invalid. Plaintiffs cannot be held liable for infringement of invalid patent claims.

115. Plaintiffs are therefore entitled to a judicial declaration that their making, using, selling, offering to sell, or importing vadadustat has not infringed and will not infringe any valid claim of the '204 patent.

COUNT VII

(Declaratory Judgment of Invalidity of U.S. Patent No. 9,920,011)

116. Plaintiffs reassert and reallege Paragraphs 1-115 of this Complaint.

117. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding the validity of the '011 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to the '011 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '011 patent. Upon information and belief, Defendants contend that the claims of the '011 patent are valid.

118. The '204, '011, '131, '012, '646, '013, and '090 patents belong to the same patent family, and the '011, '131, '012, '646, '013, and '090 patents all claim priority, either directly or indirectly, to the '204 patent.

119. Claim 1 is the only independent claim in the '011 patent. Independent claim 1 of the '011 patent recites a "method for overcoming or ameliorating cytokine-induced impairment of erythropoiesis in a subject in need thereof, the method comprising administering to the subject

an effective amount of a heterocyclic carboxamide compound that stabilizes hypoxia inducible factor α (HIFα), thereby overcoming or ameliorating the cytokine-induced impairment of erythropoiesis in the subject."

120. The claims of the '011 patent are invalid for failure to comply with one or more of the conditions of patentability under Title 35 of the United States Code and related judicial doctrines, including but not limited to 35 U.S.C. §§ 101, 102, 103, and/or 112 and/or obviousness-type double patenting.

121. For example, the claims of the '011 patent are invalid under 35 U.S.C. § 112 because the patent specification fails to provide a written description that conveys with reasonable clarity to a person of ordinary skill in the art that, as of its effective filing date, the purported inventors of the '011 patent were in possession of the subject matter claimed therein. The '011 patent claims are also invalid under 35 U.S.C. § 112 because the specification fails to provide an enabling disclosure that teaches a person of ordinary skill in the art how to make and use the full scope of the claimed subject matter without undue experimentation.

122. The specification of the '011 patent merely provides biological testing data for at most 4 exemplary compounds, Compounds A-D. '011 patent, Examples 1-9, 11, 15, 17, 19, 20, 21. In stark contrast, generic Formula I disclosed by the '011 patent encompasses a "staggeringly large" number of compounds—on the order of at least 10^{183}—and is merely an alleged example of the claimed "heterocyclic carboxamide compound." *Akebia Therapeutics, Inc. v. FibroGen, Inc.*, [2020] EWHC 866 (Pat), ¶ 368 (Apr. 20, 2020). There is no teaching or guidance within the specification with regard to which of these 10^{183} molecules referenced in the specification, beyond the 4 allegedly exemplary compounds, have the claimed functional

property of "overcoming or ameliorating cytokine-induced impairment of erythropoiesis in a subject in need thereof" or "stabiliz[ing] hypoxia inducible factor α (HIFα)."

123. The claimed genus of "a heterocyclic carboxamide compound" encompasses a vast number of compounds. The specification does not provide sufficient written description to support that such a vast number of compounds within the genus of "a heterocyclic carboxamide compound" are capable of achieving the claimed function of "overcoming or ameliorating cytokine-induced impairment of erythropoiesis in a subject in need thereof" or "stabiliz[ing] hypoxia inducible factor α (HIFα)," especially given the unpredictability of the pharmaceutical field. In addition, at the effective filing date of the '011 patent, a person of ordinary skill in the art would have been required to engage in undue experimentation to determine which of the vast number of compounds within the genus of "a heterocyclic carboxamide compound" could achieve the claimed functions, given the unpredictability of the pharmaceutical field.

124. Thus, the specification fails to demonstrate that the applicant possessed or enabled the full scope of the claims to the functionally-defined genus.

125. To the extent that Defendants assert that the claims of the '011 patent are supported by the specification, the claims would have been anticipated under 35 U.S.C. § 102 and/or obvious under 35 U.S.C. § 103 because the broad, functionally claimed genus of HIF-PHIs was known and/or obvious in view of the prior art, which includes, but is not limited to, WO 2002/074981; Ivan et al., Science, 292, 464-468, 2001; Ivan et al., PNAS, Vol. 99, 13459-13464, 2002; Epstein et al., Cell, Vol. 107, 43-54, October 5, 2001; WO2003/053997; and Wiesener et al., Ann. Med. 2003, 35, 183-190.

126. In addition, the '011 patent is also invalid because it claims subject matter that is obvious in light of claims of FibroGen's patents that expire earlier. For example, the '011 patent

will expire on June 3, 2024, and the '172 patent will expire on December 6, 2022. The claims of the '011 patent are not patentably distinct from the claims of the '172 patent. The claims of the '011 patent recite methods "for overcoming or ameliorating cytokine-induced impairment of erythropoiesis in a subject in need thereof," "comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes hypoxia inducible factor α (HIFα), thereby overcoming or ameliorating the cytokine-induced impairment of erythropoiesis in the subject." Claim 1 of the '172 patent recites a "method for treating a hypoxic or ischemic disorder or condition in a subject," "comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia inducible factor (HIFα)." The '172 patent further describes that "[t]he ability of the methods of the invention to increase both endogenous erythropoietin and transport and utilization of iron provides specific advantage in oxygen delivery in both normoxic and hypoxic environments." '172 patent, 40:4-7. Thus, claims 1-6 of the '011 patent are obvious in view of claim 1 of the '172 patent. Therefore, the claims of the '011 patent are invalid for obviousness-type double patenting in view of claim 1 of the '172 patent.

127. Plaintiffs therefore are entitled to a judicial declaration that the claims of the '011 patent are invalid.

COUNT VIII

(Declaratory Judgment of Noninfringement of U.S. Patent No. 9,920,011)

128. Plaintiffs repeat and reallege Paragraphs 1-127 of this Complaint.

129. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding infringement of the '011 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the

parties relating to foreign counterparts to the '011 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '011 patent.

130. Plaintiffs' manufacture, use, sale, offer for sale, or importation of vadadustat has not infringed and will not infringe, either directly or indirectly, any valid claim of the '011 patent, either literally or under the doctrine of equivalents.

131. For example, claim 1 is the only independent claim in the '011 patent. Claim 1 recites a "method for overcoming or ameliorating cytokine-induced impairment of erythropoiesis in a subject in need thereof." Akebia is not seeking FDA approval for vadadustat for any indication for overcoming or ameliorating cytokine-induced impairment of erythropoiesis. The use of vadadustat in accordance with its proposed label therefore will not infringe any claim of the '011 patent, and Plaintiffs' marketing of vadadustat for use in accordance with its proposed label will not induce or contribute to infringement of any claim of the '011 patent.

132. In addition, the specification for the '011 patent does not disclose the structure of vadadustat or any data for vadadustat. There is no disclosure in the '011 patent that would have led a person of ordinary skill in the art to use vadadustat to practice the claimed methods. To the extent that Defendants assert that the claims of the '011 patent nevertheless encompass the use of vadadustat, the claims of the '011 patent would be invalid for lack of adequate written description and lack of enablement under 35 U.S.C. § 112.

133. Finally, for at least the reasons described above in Count VII, the claims of the '011 patent are invalid. Plaintiffs cannot be held liable for infringement of invalid patent claims.

134. Plaintiffs are therefore entitled to a judicial declaration that their making, using, selling, offering to sell, or importing vadadustat has not infringed and will not infringe any valid claim of the ’011 patent.

COUNT IX

(Declaratory Judgment of Invalidity of U.S. Patent No. 8,629,131)

135. Plaintiffs reassert and reallege Paragraphs 1-134 of this Complaint.

136. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding the validity of the ’131 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the ’131 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the ’131 patent. Upon information and belief, Defendants contend that the claims of the ’131 patent are valid.

137. The ’204, ’011, ’131, ’012, ’646, ’013, and ’090 patents belong to the same patent family, and the ’011, ’131, ’012, ’646, ’013, and ’090 patents all claim priority, either directly or indirectly, to the ’204 patent.

138. Claim 1 is the only independent claim in the ’131 patent. Independent claim 1 of the ’131 patent recites a “method for increasing iron absorption in a subject in need thereof, the method comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia-inducible factor (HIFα), thereby increasing iron absorption in the subject.”

139. The claims of the ’131 patent are invalid for failure to comply with one or more of the conditions of patentability under Title 35 of the United States Code and related judicial

doctrines, including but not limited to 35 U.S.C. §§ 101, 102, 103, and/or 112 and/or obviousness-type double patenting.

140. For example, the claims of the '131 patent are invalid under 35 U.S.C. § 112 because the patent specification fails to provide a written description that conveys with reasonable clarity to a person of ordinary skill in the art that, as of its effective filing date, the purported inventors of the '131 patent were in possession of the subject matter claimed therein. The claims of the '131 patent are also invalid under 35 U.S.C. § 112 because the specification fails to provide an enabling disclosure that teaches a person of ordinary skill in the art how to make and use the full scope of the claimed subject matter without undue experimentation. At least claim 9 of the '131 patent is also indefinite for failing to particularly point out and distinctly claim the subject matter of the alleged invention.

141. The specification of the '131 patent merely provides biological testing data for at most 4 exemplary compounds, Compounds A-D. '131 patent, Examples 1-9, 11, 15, 17, 19, 20, 21. In stark contrast, generic Formula I disclosed by the '131 patent encompasses a "staggeringly large" number of compounds—on the order of at least 10^{183}—and is merely an alleged example of the claimed "heterocyclic carboxamide compound." *Akebia Therapeutics, Inc. v. FibroGen, Inc.*, [2020] EWHC 866 (Pat), ¶ 368 (Apr. 20, 2020). There is no teaching or guidance within the specification with regard to which of these 10^{183} molecules referenced in the specification, beyond the 4 allegedly exemplary compounds, have the claimed functional property of "increasing iron absorption in a subject" or "stabiliz[ing] the alpha subunit of hypoxia-inducible factor (HIFα)."

142. The claimed genus of "a heterocyclic carboxamide compound" encompasses a vast number of compounds. The specification does not provide sufficient written description to

support that such a vast number of compounds within the genus of "a heterocyclic carboxamide compound" are capable of achieving the claimed function of "increasing iron absorption in a subject" or "stabiliz[ing] the alpha subunit of hypoxia-inducible factor (HIFα)," especially given the unpredictability of the pharmaceutical field. In addition, at the effective filing date of the '131 patent, a person of ordinary skill in the art would have been required to engage in undue experimentation to determine which of the vast number of compounds within the genus of "a heterocyclic carboxamide compound" could achieve the claimed functions, given the unpredictability of the pharmaceutical field.

143. Thus, the specification fails to demonstrate that the applicant possessed or enabled the full scope of the claims to the functionally-defined genus.

144. Additionally, claim 9 of the '131 patent recites "a structural mimetic of 2-oxoglutarate," for which the specification provides no structural definition, merely stating that such compounds optionally "may inhibit the target 2-oxoglutarate dioxygenase enzyme family member competitively with respect to 2-oxoglutarate and noncompetitively with respect to iron." '131 patent, 27:26-28. Thus, claim 9 is indefinite because a person of ordinary skill in the art would not be able to understand the bounds of that limitation with reasonable certainty.

145. To the extent that Defendants assert that the claims of the '131 patent are supported by the specification, the claims would have been anticipated under 35 U.S.C. § 102 and/or obvious under 35 U.S.C. § 103 because the broad, functionally claimed genus of HIF-PHIs was known and/or obvious in view of the prior art, which includes, but is not limited to, WO 2002/074981; Ivan et al., Science, 292, 464-468, 2001; Ivan et al., PNAS, Vol. 99, 13459-13464, 2002; Epstein et al., Cell, Vol. 107, 43-54, October 5, 2001; WO2003/053997; and Wiesener et al., Ann. Med. 2003, 35, 183-190.

146. In addition, the '131 patent is also invalid because it claims subject matter that is obvious in light of claims of FibroGen's patents that expire earlier. For example, the '131 patent will expire on June 3, 2024, and the '172 patent will expire on December 6, 2022. The claims of the '131 patent are not patentably distinct from the claims of the '172 patent. The claims of the '131 patent recite methods "for increasing iron absorption in a subject in need thereof," "comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia-inducible factor (HIFα), thereby increasing iron absorption in the subject." Claim 1 of the '172 patent recites a "method for treating a hypoxic or ischemic disorder or condition in a subject," "comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia inducible factor (HIFα)." The '172 patent further describes that "[t]he ability of the methods of the invention to increase both endogenous erythropoietin and transport and utilization of iron provides specific advantage in oxygen delivery in both normoxic and hypoxic environments." '172 patent, 40:4-7. Thus, claims 1-11 of the '131 patent are obvious in view of claim 1 of the '172 patent. Therefore, the claims of the '131 patent are invalid for obviousness-type double patenting in view of claim 1 of the '172 patent.

147. Plaintiffs therefore are entitled to a judicial declaration that the claims of the '131 patent are invalid.

COUNT X

(Declaratory Judgment of Noninfringement of U.S. Patent No. 8,629,131)

148. Plaintiffs repeat and reallege Paragraphs 1-147 of this Complaint.

149. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding infringement of the '131 patent. Upon obtaining FDA approval, Plaintiffs

intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '131 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '131 patent.

150. Plaintiffs' manufacture, use, sale, offer for sale, or importation of vadadustat has not infringed and will not infringe, either directly or indirectly, any valid claim of the '131 patent, either literally or under the doctrine of equivalents.

151. For example, claim 1 is the only independent claim in the '131 patent. Claim 1 recites a "method for increasing iron absorption." Akebia is not seeking FDA approval for vadadustat for any indication for increasing iron absorption. The use of vadadustat in accordance with its proposed label therefore will not infringe any claim of the '131 patent, and Plaintiffs' marketing of vadadustat for use in accordance with its proposed label will not induce or contribute to infringement of any claim of the '131 patent.

152. In addition, the specification for the '131 patent does not disclose the structure of vadadustat or any data for vadadustat. There is no disclosure in the '131 patent that would have led a person of ordinary skill in the art to use vadadustat to practice the claimed methods. To the extent that Defendants assert that the claims of the '131 patent nevertheless encompass the use of vadadustat, the claims of the '131 patent would be invalid for lack of adequate written description and lack of enablement under 35 U.S.C. § 112.

153. Finally, for at least the reasons described above in Count IX, the claims of the '131 patent are invalid. Plaintiffs cannot be held liable for infringement of invalid patent claims.

154. Plaintiffs are therefore entitled to a judicial declaration that their making, using, selling, offering to sell, or importing vadadustat has not infringed and will not infringe any valid claim of the '131 patent.

COUNT XI

(Declaratory Judgment of Invalidity of U.S. Patent No. 8,604,012)

155. Plaintiffs repeat and reallege Paragraphs 1-154 of this Complaint.

156. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding the validity of the '012 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '012 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '012 patent. Upon information and belief, Defendants contend that the claims of the '012 patent are valid.

157. The '204, '011, '131, '012, '646, '013, and '090 patents belong to the same patent family, and the '011, '131, '012, '646, '013, and '090 patents all claim priority, either directly or indirectly, to the '204 patent.

158. Claim 1 is the only independent claim in the '012 patent. Independent claim 1 of the '012 patent recites a "method for increasing serum iron in a subject in need thereof, the method comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia-inducible factor (HIFα), thereby increasing serum iron in the subject."

159. The claims of the '012 patent are invalid for failure to comply with one or more of the conditions of patentability under Title 35 of the United States Code and related judicial

doctrines, including but not limited to 35 U.S.C. §§ 101, 102, 103, and/or 112 and/or obviousness-type double patenting.

160. For example, the claims of the '012 patent are invalid under 35 U.S.C. § 112 because the patent specification fails to provide a written description that conveys with reasonable clarity to a person of ordinary skill in the art that, as of its effective filing date, the purported inventors of the '012 patent were in possession of the subject matter claimed therein. The claims of the '012 patent are also invalid under 35 U.S.C. § 112 because the specification fails to provide an enabling disclosure that teaches a person of ordinary skill in the art how to make and use the full scope of the claimed subject matter without undue experimentation. At least claim 11 of the '012 patent is also indefinite for failing to particularly point out and distinctly claim the subject matter of the alleged invention.

161. The specification of the '012 patent merely provides biological testing data for at most 4 exemplary compounds, Compounds A-D. '012 patent, Examples 1-9, 11, 15, 17, 19, 20, 21. In stark contrast, generic Formula I disclosed by the '012 patent encompasses a "staggeringly large" number of compounds—on the order of at least 10^{183}—and is merely an alleged example of the claimed "heterocyclic carboxamide compound." *Akebia Therapeutics, Inc. v. FibroGen, Inc.*, [2020] EWHC 866 (Pat), ¶ 368 (Apr. 20, 2020). There is no teaching or guidance within the specification with regard to which of these 10^{183} molecules referenced in the specification, beyond the 4 allegedly exemplary compounds, have the claimed functional property of "increasing serum iron in a subject in need thereof" or "stabiliz[ing] the alpha subunit of hypoxia-inducible factor (HIFα)."

162. The claimed genus of "a heterocyclic carboxamide compound" encompasses a vast number of compounds. The specification does not provide sufficient written description to

support that such a vast number of compounds within the genus of "a heterocyclic carboxamide compound" are capable of achieving the claimed function of "increasing serum iron in a subject in need thereof" or "stabiliz[ing] the alpha subunit of hypoxia-inducible factor (HIFα)," especially given the unpredictability of the pharmaceutical field. In addition, at the effective filing date of the '012 patent, a person of ordinary skill in the art would have been required to engage in undue experimentation to determine which of the vast number of compounds within the genus of "a heterocyclic carboxamide compound" could achieve the claimed functions, given the unpredictability of the pharmaceutical field.

163. Thus, the specification fails to demonstrate that the applicant possessed or enabled the full scope of the claims to the functionally-defined genus.

164. Additionally, claim 11 of the '012 patent recites "a structural mimetic of 2-oxoglutarate," for which the specification provides no structural definition, merely stating that such compounds optionally "may inhibit the target 2-oxoglutarate dioxygenase enzyme family member competitively with respect to 2-oxoglutarate and noncompetitively with respect to iron." '012 patent, 27:24-26. Thus, claim 11 of the '012 patent is indefinite because a person of ordinary skill in the art would not be able to understand the bounds of that limitation with reasonable certainty.

165. To the extent that Defendants assert that the claims of the '012 patent are supported by the specification, the claims would have been anticipated under 35 U.S.C. § 102 and/or obvious under 35 U.S.C. § 103 because the broad, functionally claimed genus of HIF-PHIs was known and/or obvious in view of the prior art, which includes, but is not limited to, WO 2002/074981; Ivan et al., Science, 292, 464-468, 2001; Ivan et al., PNAS, Vol. 99, 13459-

13464, 2002; Epstein et al., Cell, Vol. 107, 43-54, October 5, 2001; WO2003/053997; and Wiesener et al., Ann. Med. 2003, 35, 183-190.

166. In addition, the '012 patent is also invalid because it claims subject matter that is obvious in light of claims of FibroGen's patents that expire earlier. For example, the '012 patent will expire on June 3, 2024, and the '172 patent will expire on December 6, 2022. The claims of the '012 patent are not patentably distinct from the claims of the '172 patent. The claims of the '012 patent recite methods "for increasing serum iron in a subject in need thereof," "comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia-inducible factor (HIFα), thereby increasing serum iron in the subject." Claim 1 of the '172 patent recites a "method for treating a hypoxic or ischemic disorder or condition in a subject," "comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia inducible factor (HIFα)." The '172 patent further describes that "[t]he ability of the methods of the invention to increase both endogenous erythropoietin and transport and utilization of iron provides specific advantage in oxygen delivery in both normoxic and hypoxic environments." Thus, claims 1-11 of the '012 patent are obvious in view of claim 1 of the '172 patent. Therefore, the claims of the '012 patent are invalid for obviousness-type double patenting in view of claim 1 of the '172 patent.

167. Plaintiffs therefore are entitled to a judicial declaration that the claims of the '012 patent are invalid.

COUNT XII

(Declaratory Judgment of Noninfringement of U.S. Patent No. 8,604,012)

168. Plaintiffs repeat and reallege Paragraphs 1-167 of this Complaint.

169. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding infringement of the '012 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '012 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States will infringe the '012 patent.

170. Plaintiffs' manufacture, use, sale, offer for sale, or importation of vadadustat has not infringed and will not infringe, either directly or indirectly, any valid claim of the '012 patent, either literally or under the doctrine of equivalents.

171. For example, claim 1 is the only independent claim in the '012 patent. Claim 1 recites a "method for increasing serum iron." Akebia is not seeking FDA approval for vadadustat for any indication to increase serum iron. In fact, during prosecution of the '204 patent, a family member of the '012 patent, FibroGen distinguished the treatment of anemia associated with chronic kidney disease (i.e., the proposed indication of vadadustat) from the methods of treatment claimed in the '012 patent. *See* File History for U.S. Patent Appl. No., 10/861,590, Response to Office Action at 15-17 (Sept. 25, 2009). The use of vadadustat in accordance with its proposed label therefore will not infringe any claim of the '012 patent, and Plaintiffs' marketing of vadadustat for use in accordance with its proposed label will not induce or contribute to infringement of any claim of the '012 patent.

172. In addition, the specification for the '012 patent does not disclose the structure of vadadustat or any data for vadadustat. There is no disclosure in the '012 patent that would have led a person of ordinary skill in the art to use vadadustat to practice the claimed methods. To the extent that FibroGen asserts that the claims of the '012 patent nevertheless encompass the use of

vadadustat, the claims of the '012 patent would be invalid for lack of adequate written description and lack of enablement under 35 U.S.C. § 112.

173. Finally, for at least the reasons described above in Count XI, the claims of the '012 patent are invalid. Plaintiffs cannot be held liable for infringement of invalid patent claims.

174. Plaintiffs are therefore entitled to a judicial declaration that their making, using, selling, offering to sell, or importing vadadustat has not infringed and will not infringe any valid claim of the '012 patent.

COUNT XIII

(Declaratory Judgment of Invalidity of U.S. Patent No. 8,609,646)

175. Plaintiffs reassert and reallege Paragraphs 1-174 of this Complaint.

176. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding the validity of the '646 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '646 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '646 patent. Upon information and belief, Defendants contend that the claims of the '646 patent are valid.

177. The '204, '011, '131, '012, '646, '013, and '090 patents belong to the same patent family, and the '011, '131, '012, '646, '013, and '090 patents all claim priority, either directly or indirectly, to the '204 patent.

178. Claim 1 is the only independent claim of the '646 patent. Independent claim 1 of the '646 patent recites a "method for decreasing hepcidin expression in a subject in need thereof,

the method comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia-inducible factor (HIFα), thereby decreasing hepcidin expression in the subject."

179. The claims of the '646 patent are invalid for failure to comply with one or more of the conditions of patentability under Title 35 of the United States Code and related judicial doctrines, including but not limited to 35 U.S.C. §§ 101, 102, 103, and/or 112 and/or obviousness-type double patenting.

180. For example, the claims of the '646 patent are invalid under 35 U.S.C. § 112 because the patent specification fails to provide a written description that conveys with reasonable clarity to a person of ordinary skill in the art that, as of its effective filing date, the purported inventors of the '646 patent were in possession of the subject matter claimed therein. The claims of the '646 patent are also invalid under 35 U.S.C. § 112 because the specification fails to provide an enabling disclosure that teaches a person of ordinary skill in the art how to make and use the full scope of the claimed subject matter without undue experimentation. At least claim 9 of the '646 patent is also indefinite for failing to particularly point out and distinctly claim the subject matter of the alleged invention.

181. The specification of the '646 patent merely provides biological testing data for at most 4 exemplary compounds, Compounds A-D. '646 patent, Examples 1-9, 11, 15, 17, 19, 20, 21. In stark contrast, generic Formula I disclosed by the '646 patent encompasses a "staggeringly large" number of compounds—on the order of at least 10^{183}—and is merely an alleged example of the claimed "heterocyclic carboxamide compound." *Akebia Therapeutics, Inc. v. FibroGen, Inc.*, [2020] EWHC 866 (Pat), ¶ 368 (Apr. 20, 2020). There is no teaching or guidance within the specification with regard to which of these 10^{183} molecules referenced in the

specification, beyond the 4 allegedly exemplary compounds, have the claimed functional property of "decreasing hepcidin expression in a subject" or "stabiliz[ing] the alpha subunit of hypoxia-inducible factor (HIFα)."

182. The claimed genus of "a heterocyclic carboxamide compound" encompasses a vast number of compounds. The specification does not provide sufficient written description to support that such a vast number of compounds within the genus of "a heterocyclic carboxamide compound" are capable of achieving the claimed function of "decreasing hepcidin expression in a subject" or "stabiliz[ing] the alpha subunit of hypoxia-inducible factor (HIFα)," especially given the unpredictability of the pharmaceutical field. In addition, at the effective filing date of the '646 patent, a person of ordinary skill in the art would have been required to engage in undue experimentation to determine which of the vast number of compounds within the genus of "a heterocyclic carboxamide compound" could achieve the claimed functions, given the unpredictability of the pharmaceutical field.

183. Thus, the specification fails to demonstrate that the applicant possessed or enabled the full scope of the claims to the functionally-defined genus.

184. Additionally, claim 9 of the '646 patent recites "a structural mimetic of 2-oxoglutarate," for which the specification provides no structural definition, merely stating that such compounds optionally "may inhibit the target 2-oxoglutarate dioxygenase enzyme family member competitively with respect to 2-oxoglutarate and noncompetitively with respect to iron." '646 patent, 27:24-26. Thus, claim 9 of the '646 patent is indefinite because a person of ordinary skill in the art would not be able to understand the bounds of that limitation with reasonable certainty.

185. To the extent that Defendants assert that the claims of the '646 patent are supported by the specification, the claims would have been anticipated under 35 U.S.C. § 102 and/or obvious under 35 U.S.C. § 103 because the broad, functionally claimed genus of HIF-PHIs was known and/or obvious in view of the prior art, which includes, but is not limited to, WO 2002/074981; Ivan et al., Science, 292, 464-468, 2001; Ivan et al., PNAS, Vol. 99, 13459-13464, 2002; Epstein et al., Cell, Vol. 107, 43-54, October 5, 2001; WO2003/053997; and Wiesener et al., Ann. Med. 2003, 35, 183-190.

186. In addition, the '646 patent is also invalid because it claims subject matter that is obvious in light of claims of FibroGen's patents that expire earlier. For example, the '646 patent will expire on June 3, 2024, and the '172 patent will expire on December 6, 2022. The claims of the '646 patent are not patentably distinct from the claims of the '172 patent. The claims of the '646 patent recites methods "for decreasing hepcidin expression in a subject in need thereof," "comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia-inducible factor (HIFα), thereby decreasing hepcidin expression in the subject." Claim 1 of the '172 patent recites a "method for treating a hypoxic or ischemic disorder or condition in a subject," "comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia inducible factor (HIFα)." The '172 patent further describes that "[t]he ability of the methods of the invention to increase both endogenous erythropoietin and transport and utilization of iron provides specific advantage in oxygen delivery in both normoxic and hypoxic environments." Thus, claims 1-9 of the '646 patent are obvious in view of claim 1 of the '172 patent. Therefore, the claims of the '646 patent are invalid for obviousness-type double patenting in view of claim 1 of the '172 patent.

187. Plaintiffs therefore are entitled to a judicial declaration that the claims of the '646 patent are invalid.

COUNT XIV

(Declaratory Judgment of Noninfringement of U.S. Patent No. 8,609,646)

188. Plaintiffs repeat and reallege Paragraphs 1-187 of this Complaint.

189. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding infringement of the '646 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '646 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '646 patent.

190. Plaintiffs' manufacture, use, sale, offer for sale, or importation of vadadustat has not infringed and will not infringe, either directly or indirectly, any valid claim of the '646 patent, either literally or under the doctrine of equivalents.

191. For example, claim 1 is the only independent claim in the '646 patent. Claim 1 recites a "method for decreasing hepcidin expression in a subject in need thereof." Akebia is not seeking FDA approval for vadadustat for any indication for decreasing hepcidin expression. The use of vadadustat in accordance with its proposed label therefore will not infringe any claim of the '646 patent, and Plaintiffs' marketing of vadadustat for use in accordance with its proposed label will not induce or contribute to infringement of any claim of the '646 patent.

192. In addition, the specification for the '646 patent does not disclose the structure of vadadustat or any data for vadadustat. There is no disclosure in the '646 patent that would have led a person of ordinary skill in the art to use vadadustat to practice the claimed methods. To the

extent that Defendants assert that the claims of the '646 patent nevertheless encompass the use of vadadustat, the claims of the '646 patent would be invalid for lack of adequate written description and lack of enablement under 35 U.S.C. § 112.

193. Finally, for at least the reasons described above in Count XIII, the claims of the '646 patent are invalid. Plaintiffs cannot be held liable for infringement of invalid patent claims.

194. Plaintiffs are therefore entitled to a judicial declaration that their making, using, selling, offering to sell, or importing vadadustat has not infringed and will not infringe any valid claim of the '646 patent.

COUNT XV

(Declaratory Judgment of Invalidity of U.S. Patent No. 8,604,013)

195. Plaintiffs reassert and reallege Paragraphs 1-194 of this Complaint.

196. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding the validity of the '013 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '013 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '013 patent. Upon information and belief, Defendants contend that the claims of the '013 patent are valid.

197. The '204, '011, '131, '012, '646, '013, and '090 patents belong to the same patent family, and the '011, '131, '012, '646, '013, and '090 patents all claim priority, either directly or indirectly, to the '204 patent.

198. Claim 1 is the only independent claim in the '013 patent. Independent claim 1 of the '013 patent recites a "method for treating anemia in a subject in need thereof, the method comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia-inducible factor (HIFα), thereby increasing the percent transferrin saturation in the subject, wherein the subject is a subject having a percent transferrin saturation level below 20% prior to said administering."

199. The claims of the '013 patent are invalid for failure to comply with one or more of the conditions of patentability under Title 35 of the United States Code and related judicial doctrines, including but not limited to 35 U.S.C. §§ 101, 102, 103, and/or 112 and/or obviousness-type double patenting.

200. For example, the claims of the '013 patent are invalid under 35 U.S.C. § 112 because the patent specification fails to provide a written description that conveys with reasonable clarity to a person of ordinary skill in the art that, as of its effective filing date, the purported inventors of the '013 patent were in possession of the subject matter claimed therein. The claims of the '013 patent are also invalid under 35 U.S.C. § 112 because the specification fails to provide an enabling disclosure that teaches a person of ordinary skill in the art how to make and use the full scope of the claimed subject matter without undue experimentation. At least claim 13 of the '013 patent is also indefinite for failing to particularly point out and distinctly claim the subject matter of the alleged invention.

201. The specification of the '013 patent merely provides biological testing data for at most 4 exemplary compounds, Compounds A-D. '013 patent, Examples 1-9, 11, 15, 17, 19, 20, 21. In stark contrast, generic Formula I disclosed by the '013 patent encompasses a "staggeringly large" number of compounds—on the order of at least 10^{183}—and is merely an

alleged example of the claimed "heterocyclic carboxamide compound." *Akebia Therapeutics, Inc. v. FibroGen, Inc.*, [2020] EWHC 866 (Pat), ¶ 368 (Apr. 20, 2020). There is no teaching or guidance within the specification with regard to which of these 10^{183} molecules referenced in the specification, beyond those 4 allegedly exemplary compounds, have the claimed functional property of "treating anemia in a subject," "stabiliz[ing] the alpha subunit of hypoxia-inducible factor (HIFα)," or "increasing the percent transferrin saturation in the subject."

202. The claimed genus of "a heterocyclic carboxamide compound" encompasses a vast number of compounds. The specification does not provide sufficient written description to support that such a vast number of compounds within the genus of "a heterocyclic carboxamide compound" are capable of achieving the claimed function of "treating anemia in a subject," "stabiliz[ing] the alpha subunit of hypoxia-inducible factor (HIFα)," or "increasing the percent transferrin saturation in the subject," especially given the unpredictability of the pharmaceutical field. In addition, at the effective filing date of the '013 patent, a person of ordinary skill in the art would have been required to engage in undue experimentation to determine which of the vast number of compounds within the genus of "a heterocyclic carboxamide compound" could achieve the claimed functions, given the unpredictability of the pharmaceutical field.

203. Thus, the specification fails to demonstrate that the applicant possessed or enabled the full scope of the claims to the functionally-defined genus.

204. Additionally, claim 13 of the '013 patent recites "a structural mimetic of 2-oxoglutarate," for which the specification provides no structural definition, merely stating that such compounds optionally "may inhibit the target 2-oxoglutarate dioxygenase enzyme family member competitively with respect to 2-oxoglutarate and noncompetitively with respect to iron." '013 patent, 27:26-28. Thus, claim 13 of the '013 patent is indefinite because a person of

ordinary skill in the art would not be able to understand the bounds of that limitation with reasonable certainty.

205. To the extent that Defendants assert that the claims of the '013 patent are supported by the specification, the claims would have been anticipated under 35 U.S.C. § 102 and/or obvious under 35 U.S.C. § 103 because the broad, functionally claimed genus of HIF-PHIs was known and/or obvious in view of the prior art, which includes, but is not limited to, WO 2002/074981; Ivan et al., Science, 292, 464-468, 2001; Ivan et al., PNAS, Vol. 99, 13459-13464, 2002; Epstein et al., Cell, Vol. 107, 43-54, October 5, 2001; WO2003/053997; and Wiesener et al., Ann. Med. 2003, 35, 183-190.

206. In addition, the '013 patent is also invalid because it claims subject matter that is obvious in light of claims of FibroGen's patents that expire earlier. For example, the '013 patent will expire on June 3, 2024, and the '172 patent will expire on December 6, 2022. The claims of the '013 patent are not patentably distinct from the claims of the '172 patent. The claims of the '013 patent recites methods "for treating anemia in a subject in need thereof," "comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia-inducible factor (HIFα), thereby increasing the percent transferrin saturation in the subject, wherein the subject is a subject having a percent transferrin saturation level below 20% prior to said administering." Claim 1 of the '172 patent recites a "method for treating a hypoxic or ischemic disorder or condition in a subject," "comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia inducible factor (HIFα)." Thus, claims 1-13 of the '013 patent are obvious in view of claim 1 of the '172 patent. Therefore, the claims of the '013 patent are invalid for obviousness-type double patenting in view of claim 1 of the '172 patent.

207. Plaintiffs therefore are entitled to a judicial declaration that the claims of the '013 patent are invalid.

COUNT XVI

(Declaratory Judgment of Noninfringement of U.S. Patent No. 8,604,013)

208. Plaintiffs repeat and reallege Paragraphs 1-207 of this Complaint.

209. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding infringement of the '013 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '013 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '013 patent.

210. Plaintiffs' manufacture, use, sale, offer for sale, or importation of vadadustat has not infringed and will not infringe, either directly or indirectly, any valid claim of the '013 patent, either literally or under the doctrine of equivalents.

211. For example, claim 1 is the only independent claim in the '013 patent. Claim 1 recites a "method for treating anemia" by "increasing the percent transferrin saturation in the subject, wherein the subject is a subject having a percent transferrin saturation level below 20% prior to said administering." Akebia is not seeking FDA approval for vadadustat for any indication for increasing the percent transferrin saturation in the subject, wherein the subject is a subject having a percent transferrin saturation level below 20% prior to said administering. The use of vadadustat in accordance with its proposed label therefore will not infringe any claim of the '013 patent, and Plaintiffs' marketing of vadadustat for use in accordance with its proposed label will not induce or contribute to infringement of any claim of the '013 patent.

212. In addition, the specification for the '013 patent does not disclose the structure of vadadustat or any data for vadadustat. There is no disclosure in the '013 patent that would have led a person of ordinary skill in the art to use vadadustat to practice the claimed methods. To the extent that Defendants assert that the claims of the '013 patent nevertheless encompass the use of vadadustat, the claims of the '013 patent would be invalid for lack of adequate written description and lack of enablement under 35 U.S.C. § 112.

213. Finally, for at least the reasons described above in Count XV, the claims of the '013 patent are invalid. Plaintiffs cannot be held liable for infringement of invalid patent claims.

214. Plaintiffs are therefore entitled to a judicial declaration that their making, using, selling, offering to sell, or importing vadadustat has not infringed and will not infringe any valid claim of the '013 patent.

COUNT XVII

(Declaratory Judgment of Invalidity of the U.S. Patent No. 10,626,090)

215. Plaintiffs reassert and reallege Paragraphs 1-214 of this Complaint.

216. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding the validity of the '090 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '090 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '090 patent. Upon information and belief, Defendants contend that the claims of the '090 patent are valid.

217. The ’204, ’011, ’131, ’012, ’646, ’013, and ’090 patents belong to the same patent family, and the ’011, ’131, ’012, ’646, ’013, and ’090 patents all claim priority, either directly or indirectly, to the ’204 patent.

218. Claim 1 is the only independent claim in the ’090 patent. Independent claim 1 of the ’090 patent recites a “method for increasing iron absorption in a subject in need thereof,” “comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia-inducible factor (HIFsα), thereby increasing iron absorption in the subject, wherein the heterocyclic carboxamide compound is a compound of Formula I,” where the substituents in Formula I are broadly defined. Indeed, the list of potential chemical groups that may be incorporated within that generic chemical structure spans 10 columns of text in the patent. *See* ’090 patent, columns 63-72.

219. The claims of the ’090 patent are invalid for failure to comply with one or more of the conditions of patentability under Title 35 of the United States Code and related judicial doctrines, including but not limited to 35 U.S.C. §§ 101, 102, 103, and/or 112 and/or obviousness-type double patenting.

220. For example, the claims of the ’090 patent are invalid under 35 U.S.C. § 112 because the patent specification fails to provide a written description that conveys with reasonable clarity to a person of ordinary skill in the art that, as of its effective filing date, the purported inventors of the ’090 patent were in possession of the subject matter claimed therein. The claims of the ’090 patent are also invalid under 35 U.S.C. § 112 because the specification fails to provide an enabling disclosure that teaches a person of ordinary skill in the art how to make and use the full scope of the claimed subject matter without undue experimentation. At

least claim 10 of the '090 patent is also indefinite for failing to particularly point out and distinctly claim the subject matter of the alleged invention.

221. The specification of the '090 patent merely provides biological testing data for at most 4 exemplary compounds, Compounds A-D. '090 patent, Examples 1-9, 11, 15, 17, 19, 20, 21. In stark contrast, generic Formula I disclosed by the '090 patent encompasses a "staggeringly large" number of compounds—on the order of at least 10^{183}. *Akebia Therapeutics, Inc. v. FibroGen, Inc.*, [2020] EWHC 866 (Pat), ¶ 368 (Apr. 20, 2020). There is no teaching or guidance within the specification with regard to which of these 10^{183} molecules referenced in the specification, beyond the 4 allegedly exemplary compounds, have the claimed functional property of "increasing iron absorption in a subject in need thereof" or "stabiliz[ing] the alpha subunit of hypoxia-inducible factor (HIFsα)."

222. The claimed genus of "a compound of Formula I" encompasses a vast number of compounds. The specification does not provide sufficient written description to support that such a vast number of compounds within the genus of "a compound of Formula I" are capable of achieving the claimed function of "increasing iron absorption in a subject in need thereof" or "stabiliz[ing] the alpha subunit of hypoxia-inducible factor (HIFsα)," especially given the unpredictability of the pharmaceutical field. In addition, at the effective filing date of the '090 patent, a person of ordinary skill in the art would have been required to engage in undue experimentation to determine which of the vast number of compounds within the genus of "a compound of Formula I" could achieve the claimed functions, given the unpredictability of the pharmaceutical field.

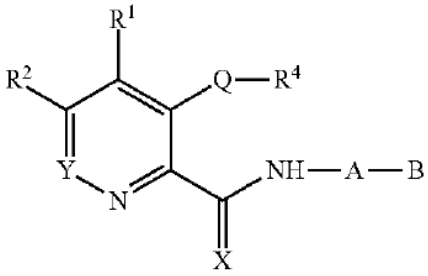
223. Thus, the specification fails to demonstrate that the applicant possessed or enabled the full scope of the claims to the functionally-defined genus.

224. Additionally, claim 10 of the '090 patent recites "a structural mimetic of 2-oxoglutarate," for which the specification provides no structural definition, merely stating that such compounds optionally "may inhibit the target 2-oxoglutarate dioxygenase enzyme family member competitively with respect to 2-oxoglutarate and noncompetitively with respect to iron." '090 patent, 28:11-14. Thus, claim 10 of the '090 patent is indefinite because a person of ordinary skill in the art would not be able to understand the bounds of that limitation with reasonable certainty.

225. To the extent that Defendants assert that the claims of the '090 patent are supported by the specification, the claims would have been anticipated under 35 U.S.C. § 102 and/or obvious under 35 U.S.C. § 103 because the broad, functionally claimed genus of HIF-PHIs was known and/or obvious in view of the prior art, which includes, but is not limited to, WO 2002/074981; Ivan et al., Science, 292, 464-468, 2001; Ivan et al., PNAS, Vol. 99, 13459-13464, 2002; Epstein et al., Cell, Vol. 107, 43-54, October 5, 2001; WO2003/053997; and Wiesener et al., Ann. Med. 2003, 35, 183-190.

226. In addition, the '090 patent is also invalid because it claims subject matter that is obvious in light of claims of FibroGen's patents that expire earlier. For example, the '090 patent will expire on June 3, 2024, and the '172 patent will expire on December 6, 2022. The claims of the '090 patent are not patentably distinct from the claims of the '172 patent. The claims of the '090 patent recites methods "for increasing iron absorption in a subject in need thereof," "comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia-inducible factor (HIFsα), thereby increasing iron absorption in the subject, wherein the heterocyclic carboxamide compound is a compound of Formula I." Claim 1 of the '172 patent recites a "method for treating a hypoxic or

ischemic disorder or condition in a subject," "comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia inducible factor (HIFα)." The '172 patent further describes that "[t]he ability of the methods of the invention to increase both endogenous erythropoietin and transport and utilization of iron provides specific advantage in oxygen delivery in both normoxic and hypoxic environments." The '172 patent also provides compounds of Formula I



which are heterocyclic carboxamide compounds, as "compounds used in the methods of the invention." '172 patent, 7:11-15:64. Thus, claims 1-10 of the '090 patent are obvious in view of claim 1 of the '172 patent. Therefore, the claims of the '090 patent are invalid for obviousness-type double patenting in view of claim 1 of the '172 patent.

227. Plaintiffs therefore are entitled to a judicial declaration that the claims of the '090 patent are invalid.

COUNT XVIII

(Declaratory Judgment of Noninfringement of U.S. Patent No. 10,626,090)

228. Plaintiffs repeat and reallege Paragraphs 1-227 of this Complaint.

229. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding infringement of the '090 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '090 patent, Plaintiffs reasonably expect that

Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '090 patent.

230. Plaintiffs' manufacture, use, sale, offer for sale, or importation of vadadustat has not infringed and will not infringe, either directly or indirectly, any valid claim of the '090 patent, either literally or under the doctrine of equivalents.

231. For example, claim 1 is the only independent claim in the '090 patent. Claim 1 recites a "method for increasing iron absorption." Akebia is not seeking FDA approval for vadadustat for any indication for increasing iron absorption. The use of vadadustat in accordance with its proposed label therefore will not infringe any claim of the '090 patent, and Plaintiffs' marketing of vadadustat for use in accordance with its proposed label will not induce or contribute to infringement of any claim of the '090 patent.

232. Moreover, the chemical structure recited in claim 1 requires a group called "R^2," which does not encompass an aryl group substituted with a halogen. Vadadustat contains an aryl group substituted with a halogen at that position and therefore does not include the R^2 chemical group recited in claim 1 or any of the claims of the '090 patent, which all depend directly or indirectly from claim 1.

233. In addition, the specification for the '090 patent does not disclose the structure of vadadustat or any data for vadadustat. There is no disclosure in the '090 patent that would have led a person of ordinary skill in the art to use vadadustat to practice the claimed methods. To the extent that Defendants assert that the claims of the '090 patent nevertheless encompass the use of vadadustat, the claims of the '090 patent would be invalid for lack of adequate written description and lack of enablement under 35 U.S.C. § 112.

234. Finally, for at least the reasons described above in Count XVII, the claims of the '090 patent are invalid. Plaintiffs cannot be held liable for infringement of invalid patent claims.

235. Plaintiffs are therefore entitled to a judicial declaration that their making, using, selling, offering to sell, or importing vadadustat has not infringed and will not infringe any valid claim of the '090 patent.

COUNT XIX

(Declaratory Judgment of Invalidity of the U.S. Patent No. 10,894,774)

236. Plaintiffs reassert and reallege Paragraphs 1-235 of this Complaint.

237. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding the validity of the '774 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '774 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '774 patent. Upon information and belief, Defendants contend that the claims of the '774 patent are valid.

238. The '774, '827, and '081 patents all claim priority, either directly or indirectly, to the '204 patent.

239. Claims 1, 10, and 17 are the only independent claims in the '774 patent. Independent claim 1 of the '774 patent recites a "method for decreasing hepcidin in a subject in need thereof, the method comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia-inducible factor (HIFα), thereby decreasing hepcidin in the subject, wherein the heterocyclic carboxamide

compound is a compound of Formula I," where the substituents in Formula I are broadly defined. Independent claim 10 of the '774 patent recites a "method for decreasing hepcidin expression in a subject in need thereof, the method comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia-inducible factor (HIFα), thereby decreasing hepcidin expression in the subject, wherein the heterocyclic carboxamide compound is a compound of Formula I," where the substituents in Formula I are broadly defined. Independent claim 17 of the '774 patent recites a "method for decreasing hepcidin expression in a subject in need thereof," "comprising administering to the subject an effective amount of a compound of Formula I," where the substituents in Formula I are broadly defined.

240. The claims of the '774 patent are invalid for failure to comply with one or more of the conditions of patentability under Title 35 of the United States Code and related judicial doctrines, including but not limited to 35 U.S.C. §§ 101, 102, 103, and/or 112 and/or obviousness-type double patenting.

241. For example, the claims of the '774 patent are invalid under 35 U.S.C. § 112 because the patent specification fails to provide a written description that conveys with reasonable clarity to a person of ordinary skill in the art that, as of its effective filing date, the purported inventors of the '774 patent were in possession of the subject matter claimed therein. The claims of the '774 patent are also invalid under 35 U.S.C. § 112 because the specification fails to provide an enabling disclosure that teaches a person of ordinary skill in the art how to make and use the full scope of the claimed subject matter without undue experimentation.

242. The specification of the '774 patent merely provides biological testing data for at most 4 exemplary compounds, Compounds A-D. '774 patent, Examples 1-9, 11, 15, 17, 19, 20,

21. In stark contrast, generic Formula I as described in the '774 patent's specification encompasses a "staggeringly large" number of compounds—on the order of at least 10^{183}. *Akebia Therapeutics, Inc. v. FibroGen, Inc.*, [2020] EWHC 866 (Pat), ¶ 368 (Apr. 20, 2020). There is no teaching or guidance within the specification with regard to which of these 10^{183} molecules referenced in the specification, beyond the 4 allegedly exemplary compounds, have the claimed functional property of "decreasing hepcidin," "decreasing hepcidin expression," or "stabiliz[ing] the alpha subunit of hypoxia-inducible factor (HIFα)."

243. The claimed genera of "a compound of Formula I" also encompass a vast number of compounds. The specification does not provide sufficient written description to support that such a vast number of compounds within the claimed genera of "a compound of Formula I" are capable of achieving the claimed function of "decreasing hepcidin," "decreasing hepcidin expression," or "stabiliz[ing] the alpha subunit of hypoxia-inducible factor (HIFα)," especially given the unpredictability of the pharmaceutical field. In addition, at the effective filing date of the '774 patent, a person of ordinary skill in the art would have been required to engage in undue experimentation to determine which of the vast number of compounds within the claimed genera of "a compound of Formula I" could achieve the claimed functions, given the unpredictability of the pharmaceutical field.

244. Additionally, claims 10-16 recite that "the heterocyclic carboxamide compound is a compound of Formula I," where the substituents in Formula I are defined therein. However, the specification of the '774 patent does not provide a written description of the Formula I defined in claims 10-16. Furthermore, claims 17-23 recite that "the heterocyclic carboxamide compound is a compound of Formula I," where the substituents in Formula I are defined therein. However, the specification of the '774 patent does not provide a written description of the

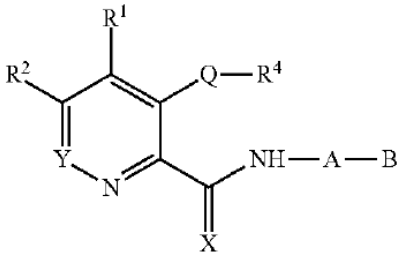
Formula I defined in claims 17-23. In fact, these claimed genera of Formula I did not appear anywhere in the specification or file history until FibroGen submitted these genera to the Patent Office in an August 21, 2020 Supplemental Amendment and Response during prosecution of the '774 patent. *See* File History for U.S. Patent Appl. No., 15/498,856, Supplemental Response (Aug. 21, 2020). Therefore, claims 10-23 are invalid for lack of written description and lack of enablement for this additional reason. To the extent that Defendants assert that claims 10-23 encompass the use of vadadustat, those claims are also anticipated and/or rendered obvious by numerous references disclosing vadadustat and its use prior to August 21, 2020.

245. Thus, the specification fails to demonstrate that the applicant possessed or enabled the full scope of the claims to the functionally-defined genera. Claims 10-23 are also invalid as anticipated and/or rendered obvious to the extent that Defendants assert that those claims encompass the use of vadadustat.

246. To the extent that Defendants assert that the claims of the '774 patent are supported by the specification, the claims would have been anticipated under 35 U.S.C. § 102 and/or obvious under 35 U.S.C. § 103 because the broad, functionally claimed genera of HIF-PHIs beyond were known and/or obvious in view of the prior art, which includes, but is not limited to, WO 2002/074981; Ivan et al., Science, 292, 464-468, 2001; Ivan et al., PNAS, Vol. 99, 13459-13464, 2002; Epstein et al., Cell, Vol. 107, 43-54, October 5, 2001; WO2003/053997; and Wiesener et al., Ann. Med. 2003, 35, 183-190.

247. In addition, the '774 patent is also invalid because it claims subject matter that is obvious in light of claims of FibroGen's patents that expire earlier. For example, the '774 patent will expire on June 3, 2024, and the '172 patent will expire on December 6, 2022. The claims of the '774 patent are not patentably distinct from the claims of the '172 patent. The claims of

the '774 patent recite methods for decreasing hepcidin or hepcidin expression, "comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia-inducible factor (HIFα)," wherein the heterocyclic carboxamide compound is a compound of Formula I. Claim 1 of the '172 patent recites a "method for treating a hypoxic or ischemic disorder or condition in a subject," "comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia inducible factor (HIFα)." The '172 patent also provides compounds of Formula I



which are heterocyclic carboxamide compounds, as "compounds used in the methods of the invention." '172 Patent, 7:11-15:64. The '172 patent further describes that "[t]he ability of the methods of the invention to increase both endogenous erythropoietin and transport and utilization of iron provides specific advantage in oxygen delivery in both normoxic and hypoxic environments." Therefore, the claims of the '774 patent are invalid for obviousness-type double patenting in view of claim 1 of the '172 patent.

248. Plaintiffs therefore are entitled to a judicial declaration that the claims of the '774 patent are invalid.

COUNT XX

(Declaratory Judgment of Noninfringement of U.S. Patent No. 10,894,774)

249. Plaintiffs repeat and reallege Paragraphs 1-248 of this Complaint.

250. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding infringement of the '774 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '774 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '774 patent.

251. Plaintiffs' manufacture, use, sale, offer for sale, or importation of vadadustat has not infringed and will not infringe, either directly or indirectly, any valid claim of the '774 patent, either literally or under the doctrine of equivalents.

252. For example, claims 1, 10, and 17 are the only independent claim in the '774 patent. Claim 1 recites a "method for decreasing hepcidin in a subject in need thereof." Claims 10 and 17 recite a "method for decreasing hepcidin expression in a subject in need thereof." Akebia is not seeking FDA approval for vadadustat for any indication for decreasing hepcidin or decreasing hepcidin expression. The use of vadadustat in accordance with its proposed label therefore will not infringe any claim of the '774 patent, and Plaintiffs' marketing of vadadustat for use in accordance with its proposed label will not induce or contribute to infringement of any claim of the '774 patent.

253. Moreover, the chemical structure recited in claims 1-16 requires a group called "R^2," which does not encompass an aryl group substituted with a halogen. Vadadustat contains an aryl group substituted with a halogen at that position and therefore does not include the R^2 chemical group recited in claims 1-16 of the '774 patent.

254. In addition, as discussed above, the specification for the '774 patent does not provide written description or enablement support for the chemical genera recited in claims 10-

23 of the ’774 patent. The chemical genera recited in claims 10-23 of the ’774 patent were first described in a claim amendment that FibroGen made on August 21, 2020 during prosecution of the ’774 patent, and those claims are not entitled to a priority date earlier than August 21, 2020. To the extent that Defendants assert that claims 10-23 encompass the use of vadadustat, those claims are anticipated and/or rendered obvious by numerous references disclosing vadadustat and its use prior to August 21, 2020.

255. Moreover, the specification for the ’774 patent does not disclose the structure of vadadustat or any data for vadadustat. There is no disclosure in the ’774 patent that would have led a person of ordinary skill in the art to use vadadustat to practice the claimed methods. To the extent that Defendants assert that the claims of the ’774 patent nevertheless encompass the use of vadadustat, the claims of the ’774 patent would be invalid for lack of adequate written description and lack of enablement under 35 U.S.C. § 112.

256. Finally, for at least the reasons described above in Count XIX, the claims of the ’774 patent are invalid. Plaintiffs cannot be held liable for infringement of invalid patent claims.

257. Plaintiffs are therefore entitled to a judicial declaration that their making, using, selling, offering to sell, or importing vadadustat has not infringed and will not infringe any valid claim of the ’774 patent.

COUNT XXI

(Declaratory Judgment of Invalidity of the U.S. Patent No. 10,882,827)

258. Plaintiffs reassert and reallege Paragraphs 1-257 of this Complaint.

259. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding the validity of the ’827 patent. Upon obtaining FDA approval, Plaintiffs

intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '827 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '827 patent. Upon information and belief, Defendants contend that the claims of the '827 patent are valid.

260. The '774, '827, and '081 patents all claim priority, either directly or indirectly, to the '204 patent.

261. Claims 1 and 3 are the only independent claims of the '827 patent. Independent claims 1 and 3 of the '827 patent recite methods "of treating anemia in a human subject comprising administering to the human subject an effective amount of a compound" "of Formula I," "wherein the human subject has a transferrin saturation (TSAT) level below 20% prior to said administering," where the substituents in Formula I are broadly defined.

262. The claims of the '827 patent are invalid for failure to comply with one or more of the conditions of patentability under Title 35 of the United States Code and related judicial doctrines, including but not limited to 35 U.S.C. §§ 101, 102, 103, and/or 112 and/or obviousness-type double patenting.

263. For example, the claims of the '827 patent are invalid under 35 U.S.C. § 112 because the patent specification fails to provide a written description that conveys with reasonable clarity to a person of ordinary skill in the art that, as of its effective filing date, the purported inventors of the '827 patent were in possession of the subject matter claimed therein. The claims of the '827 patent are also invalid under 35 U.S.C. § 112 because the specification fails to provide an enabling disclosure that teaches a person of ordinary skill in the art how to make and use the full scope of the claimed subject matter without undue experimentation.

264. The specification of the '827 patent merely provides biological testing data for at most 4 exemplary compounds, Compounds A-D. '827 patent, Examples 1-9, 11, 15, 17, 19, 20, 21. In stark contrast, generic Formula I as described in the '827 patent's specification encompasses a "staggeringly large" number of compounds—on the order of at least 10^{183}. *Akebia Therapeutics, Inc. v. FibroGen, Inc.*, [2020] EWHC 866 (Pat), ¶ 368 (Apr. 20, 2020). There is no teaching or guidance within the specification with regard to which of these 10^{183} molecules referenced in the specification, beyond the 4 allegedly exemplary compounds, have the claimed functional property of "treating anemia in a human subject" having "a transferrin saturation (TSAT) level below 20% prior to said administering."

265. The claimed genera of "a compound of Formula I" also encompasses a vast number of compounds. The specification does not provide sufficient written description to support that such a vast number of compounds within the claimed genera of "a compound of Formula I" are capable of achieving the claimed function of "treating anemia in a human subject" having "a transferrin saturation (TSAT) level below 20% prior to said administering," especially given the unpredictability of the pharmaceutical field. In addition, at the effective filing date of the '827 patent, a person of ordinary skill in the art would have been required to engage in undue experimentation to determine which of the vast number of compounds within the claimed genera of "a compound of Formula I" could achieve the claimed function, given the unpredictability of the pharmaceutical field.

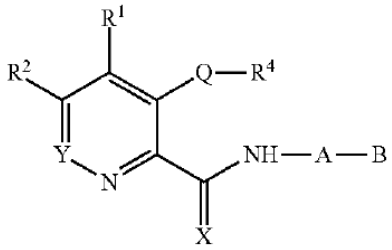
266. Additionally, claims 1-2 and 5-14 recite "a compound of Formula I," where the substituents in Formula I are defined therein. However, the specification of the '827 patent does not provide a written description of the Formula I defined in claims 1-2 and 5-14. Claims 3-4 and 15-24 recite that "a compound of Formula I," where the substituents in Formula I are defined

therein. However, the specification of the '827 patent does not provide a written description of the genera of the Formula I defined in claims 1-24. In fact, these claimed genera of Formula I did not appear anywhere in the specification or file history until FibroGen submitted these genera to the Patent Office in an August 21, 2020 Response and Amendment during prosecution of the '827 patent and/or an August 21, 2020 Response and Amendment during prosecution of the '774 patent, a family member of the '827 patent. *See* File History for U.S. Patent Appl. No., 15/498,856, Supplemental Response (Aug. 21, 2020). Claims 1-24 are invalid for lack of written description and lack of enablement for this additional reason. To the extent that Defendants assert that the claims encompass the use of vadadustat, those claims are also anticipated and/or rendered obvious by numerous references disclosing vadadustat and its use prior to August 21, 2020.

267. Thus, the specification fails to demonstrate that the applicant possessed or enabled the full scope of the claims to the functionally-defined genera. Claims 1-24 are also invalid as anticipated and/or rendered obvious to the extent that Defendants assert that those claims encompass the use of vadadustat.

268. To the extent that Defendants assert that the claims of the '827 patent are supported by the specification, the claims would have been anticipated under 35 U.S.C. § 102 and/or obvious under 35 U.S.C. § 103 because the broad, functionally claimed genera of HIF-PHIs beyond were known and/or obvious in view of the prior art, which includes, but is not limited to, WO 2002/074981; Ivan et al., Science, 292, 464-468, 2001; Ivan et al., PNAS, Vol. 99, 13459-13464, 2002; Epstein et al., Cell, Vol. 107, 43-54, October 5, 2001; WO2003/053997; and Wiesener et al., Ann. Med. 2003, 35, 183-190.

269. In addition, the ’827 patent is also invalid because it claims subject matter that is obvious in light of claims of FibroGen’s patents that expire earlier. For example, the ’827 patent will expire on March 5, 2025, and the ’172 patent will expire on December 6, 2022. The claims of the ’827 patent are not patentably distinct from the claims of the ’172 patent. The claims of the ’827 patent recites methods “for treating anemia in a human subject comprising administering to the subject an effective amount of a compound” “of Formula I,” “wherein the human subject has a transferrin saturation (TSAT) level below 20% prior to said administering.” Claim 1 of the ’172 patent recites a “method for treating a hypoxic or ischemic disorder or condition in a subject,” “comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia inducible factor (HIFα).” The ’172 patent also provides compounds of Formula I



which are heterocyclic carboxamide compounds, as “compounds used in the methods of the invention.” Thus, claims 1-24 of the ’827 patent are obvious in view of claim 1 of the ’172 patent. Therefore, the claims of the ’827 patent are invalid for obviousness-type double patenting in view of claim 1 of the ’172 patent.

270. Plaintiffs therefore are entitled to a judicial declaration that the claims of the ’827 patent are invalid.

COUNT XXII

(Declaratory Judgment of Noninfringement of U.S. Patent No. 10,882,827)

271. Plaintiffs repeat and reallege Paragraphs 1-270 of this Complaint.

272. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding infringement of the '827 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '827 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '827 patent.

273. Plaintiffs' manufacture, use, sale, offer for sale, or importation of vadadustat has not infringed and will not infringe, either directly or indirectly, any valid claim of the '827 patent, either literally or under the doctrine of equivalents.

274. For example, claims 1 and 3 are the only independent claims in the '827 patent. Claims 1 and 3 of the '827 patent recite methods "of treating anemia in a human subject comprising administering to the human subject an effective amount of a compound" "of Formula I," "wherein the human subject has a transferrin saturation (TSAT) level below 20% prior to said administering." Akebia is not seeking FDA approval for vadadustat for any indication wherein a patient has a transferrin saturation level below 20% prior to administration of the drug. The use of vadadustat in accordance with its proposed label therefore will not infringe any claim of the '827 patent, and Plaintiffs' marketing of vadadustat for use in accordance with its proposed label will not induce or contribute to infringement of any claim of the '827 patent.

275. Moreover, the chemical structure recited in claims 1-2 and 5-14 requires a group called "R^2," which does not encompass an aryl group substituted with a halogen. Vadadustat contains an aryl group substituted with a halogen at that position and therefore does not include the R^2 chemical group recited in claims 1-2 and 5-14 of the '827 patent.

276. As discussed above, the specification for the '827 patent does not provide written description support for the chemical genera recited in the claims of the '827 patent. The chemical genera recited in the claims of the '827 patent were first described in a claim amendment that FibroGen made on August 21, 2020 during prosecution of the '827 patent and/or an August 21, 2020 Response and Amendment during prosecution of the '774 patent, a family member of the '827, and those claims are not entitled to a priority date earlier than August 21, 2020. *See* File History for U.S. Patent Appl. No., 15/498,856, Supplemental Response (Aug. 21, 2020). To the extent that Defendants assert that the claims encompass the use of vadadustat, those claims are anticipated and/or rendered obvious by numerous references disclosing vadadustat and its use prior to August 21, 2020.

277. In addition, the specification for the '827 patent does not disclose the structure of vadadustat or any data for vadadustat. There is no disclosure in the '827 patent that would have led a person of ordinary skill in the art to use vadadustat to practice the claimed methods. To the extent that Defendants assert that the claims of the '827 patent nevertheless encompass the use of vadadustat, the claims of the '827 patent would be invalid for lack of adequate written description and lack of enablement under 35 U.S.C. § 112.

278. Finally, for at least the reasons described above in Count XXI, the claims of the '827 patent are invalid. Plaintiffs cannot be held liable for infringement of invalid patent claims.

279. Plaintiffs are therefore entitled to a judicial declaration that their making, using, selling, offering to sell, or importing vadadustat has not infringed and will not infringe any valid claim of the '827 patent.

COUNT XXIII

(Declaratory Judgment of Invalidity of the U.S. Patent No. 10,927,081)

280. Plaintiffs reassert and reallege Paragraphs 1-279 of this Complaint.

281. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding the validity of the '081 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '081 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '081 patent. Upon information and belief, Defendants contend that the claims of the '081 patent are valid.

282. The '774, '827, and '081 patents all claim priority, either directly or indirectly, to the '204 patent.

283. Claims 1, 13, 25, and 36 are the only independent claims in the '081 patent. Independent claims 1 and 13 of the '081 patent recite methods "of treating anemia in a human subject with kidney disease comprising administering to the human subject an effective amount of a compound of Formula I," "wherein the anemia is treated" and where the substituents in Formula I are broadly defined in two separate chemical genera for claims 1 and 13. Independent claims 25 and 36 of the '081 patent recite methods "of treating anemia in a human subject with chronic renal failure comprising administering to the human subject an effective amount of a compound of Formula I," "wherein the anemia is treated" and where the substituents in Formula I are broadly defined in two separate chemical genera for claims 25 and 36.

284. The claims of the '081 patent are invalid for failure to comply with one or more of the conditions of patentability under Title 35 of the United States Code and related judicial

doctrines, including but not limited to 35 U.S.C. §§ 101, 102, 103, and/or 112 and/or obviousness-type double patenting.

285. For example, the claims of the ’081 patent are invalid under 35 U.S.C. § 112 because the patent specification fails to provide a written description that conveys with reasonable clarity to a person of ordinary skill in the art that, as of its effective filing date, the purported inventors of the ’081 patent were in possession of the subject matter claimed therein. The claims of the ’081 patent are also invalid under 35 U.S.C. § 112 because the specification fails to provide an enabling disclosure that teaches a person of ordinary skill in the art how to make and use the full scope of the claimed subject matter without undue experimentation.

286. The specification of the ’081 patent merely provides biological testing data for at most 4 exemplary compounds, Compounds A-D. ’081 patent, Examples 1-9, 11, 15, 17, 19, 20, 21. In stark contrast, generic Formula I as described in the ’081 patent’s specification encompasses a “staggeringly large” number of compounds—on the order of at least 10^{183}. *Akebia Therapeutics, Inc. v. FibroGen, Inc.*, [2020] EWHC 866 (Pat), ¶ 368 (Apr. 20, 2020). There is no teaching or guidance within the specification with regard to which of these 10^{183} molecules referenced in the specification, beyond the 4 allegedly exemplary compounds, have the claimed functional property of “treating anemia in a human subject with kidney disease” or “treating anemia in a human subject with chronic renal failure.”

287. The claimed genera of “a compound of Formula I” also encompass a vast number of molecules. The specification does not provide sufficient written description to support that such a vast number of molecules within the claimed genus of “a compound of Formula I” are capable of achieving the claimed function of “treating anemia in a human subject with kidney disease” or “treating anemia in a human subject with chronic renal failure,” especially given the

unpredictability of the pharmaceutical field. In addition, at the effective filing date of the '081 patent, a person of ordinary skill in the art would have been required to engage in undue experimentation to determine which of the vast number of molecules within the claimed genera of "a compound of Formula I" could achieve the claimed functions, given the unpredictability of the pharmaceutical field.

288. Additionally, claims 1-12 recite methods "for treating anemia in a human subject with kidney disease comprising administering to the human subject an effective amount of a compound of Formula I," where the substituents in Formula I are defined therein. However, the specification of the '081 patent does not provide a written description of either a method for treating anemia in a human subject with kidney disease or the Formula I defined in claims 1-12.

289. Claims 13-24 recite methods "of treating anemia in a human subject with kidney disease comprising administering to the human subject an effective amount of a compound of Formula I," where the substituents in Formula I are defined therein. However, the specification of the '081 patent does not provide a written description of either a method for treating anemia in a human subject with kidney disease or the Formula I defined in claims 13-24.

290. Claims 25-35 recite methods "of treating anemia in a human subject with chronic renal failure comprising administering to the human subject an effective amount of a compound of the formula I," where the substituents in Formula I are defined therein. However, the specification of the '081 patent does not provide a written description of either a method for treating anemia in a human subject with chronic renal failure or the Formula I defined in claims 25-35.

291. Claims 36-46 recite methods "of treating anemia in a human subject with chronic renal failure comprising administering to the human subject an effective amount of a compound

of Formula I," where the substituents in Formula I are defined therein. However, the specification of the '081 patent does not provide a written description of either a method for treating anemia in a human subject with chronic renal failure or the Formula I defined in claims 36-45.

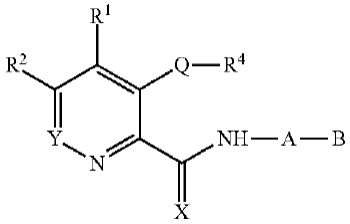
292. The specification of the '081 patent does not provide a written description of the genera of the Formula I defined in claims 1-46. In fact, these claimed genera of Formula I did not appear anywhere in the specification or file history until FibroGen submitted these genera to the Patent Office in an August 21, 2020 Response and Amendment during the prosecution of the '774 patent, a family member of the '081 patent. *See* File History for U.S. Patent Appl. No., 15/498,856, Supplemental Response (Aug. 21, 2020). Claims 1-46 are invalid for lack of written description and lack of enablement for this additional reason. To the extent that Defendants assert that the claims encompass the use of vadadustat, those claims are also anticipated and/or rendered obvious by numerous references disclosing vadadustat and its use prior to August 21, 2020.

293. Thus, the specification fails to demonstrate that the applicant possessed or enabled the full scope of the claims to the functionally-defined genera. Claims 1-46 are also invalid as anticipated and/or rendered obvious to the extent that Defendants assert that those claims encompass the use of vadadustat.

294. To the extent that Defendants assert that the claims of the '081 patent are supported by the specification, the claims would have been anticipated under 35 U.S.C. § 102 and/or obvious under 35 U.S.C. § 103 because the broad, functionally claimed genera of HIF-PHIs were known and/or obvious in view of the prior art, which includes, but is not limited to, WO 2002/074981; Ivan et al., Science, 292, 464-468, 2001; Ivan et al., PNAS, Vol. 99, 13459-

13464, 2002; Epstein et al., Cell, Vol. 107, 43-54, October 5, 2001; WO2003/053997; and Wiesener et al., Ann. Med. 2003, 35, 183-190.

295. In addition, the ’081 patent is also invalid because it claims subject matter that is obvious in light of claims of FibroGen’s patents that expire earlier. For example, the ’081 patent will expire on June 3, 2024, and the ’172 patent will expire on December 6, 2022. The claims of the ’081 patent are not patentably distinct from the claims of the ’172 patent. The claims of the ’081 patent recites methods “of treating anemia in a human subject with kidney disease comprising administering to the human subject an effective amount of a compound of Formula I.” Claims 25-46 of the ’081 patent recite methods “of treating anemia in a human subject with chronic renal failure comprising administering to the human subject an effective amount of” a compound of Formula I. Claim 1 of the ’172 patent recites a “method for treating a hypoxic or ischemic disorder or condition in a subject,” “comprising administering to the subject an effective amount of a heterocyclic carboxamide compound that stabilizes the alpha subunit of hypoxia inducible factor (HIFα).” The ’172 patent also provides compounds of Formula I



where X is O, which are heterocyclic carboxamide compounds, as “compounds used in the methods of the invention.” ’172 Patent, 7:11-15:64. Therefore, the claims of the ’081 patent are invalid for double patenting in view of claim 1 of the ’172 patent.

296. Plaintiffs therefore are entitled to a judicial declaration that the claims of the ’081 patent are invalid.

COUNT XXIV

(Declaratory Judgment of Noninfringement of U.S. Patent No. 10,927,081)

297. Plaintiffs repeat and reallege Paragraphs 1-296 of this Complaint.

298. An actual, justiciable, and continuing controversy exists between Plaintiffs and Defendants regarding infringement of the '081 patent. Upon obtaining FDA approval, Plaintiffs intend to market vadadustat in the United States. Due to the history of litigation between the parties relating to foreign counterparts to the '081 patent, Plaintiffs reasonably expect that Defendants will assert that making, using, selling, offering for sale, or importing vadadustat in the United States infringes the '081 patent.

299. Plaintiffs' manufacture, use, sale, offer for sale, or importation of vadadustat has not infringed and will not infringe, either directly or indirectly, any valid claim of the '081 patent, either literally or under the doctrine of equivalents.

300. For example, the chemical structure recited in claims 1-12 and 25-35 requires a group called "R^2," which does not encompass an aryl group substituted with a halogen. Vadadustat contains an aryl group substituted with a halogen at that position and therefore does not include the R^2 chemical group recited in claims 1-12 and 25-35 of the '081 patent.

301. As discussed above, the specification for the '081 patent does not provide written description support for the chemical genera recited in the claims of the '081 patent. The chemical generas recited in the claims of the '081 patent were first described in a claim amendment that FibroGen made on August 21, 2020 during the prosecution of the '774 patent, a family member of the '081 patent, and those claims are not entitled to a priority date earlier than August 21, 2020. To the extent that Defendants assert that the claims encompass the use of

vadadustat, those claims are anticipated and/or rendered obvious by numerous references disclosing vadadustat and its use prior to August 21, 2020.

302. In addition, the specification for the '081 patent does not disclose the structure of vadadustat or any data for vadadustat. There is no disclosure in the '081 patent that would have led a person of ordinary skill in the art to use vadadustat to practice the claimed methods. To the extent that Defendants assert that the claims of the '081 patent nevertheless encompass the use of vadadustat, the claims of the '081 patent would be invalid for lack of adequate written description and lack of enablement under 35 U.S.C. § 112.

303. Finally, for at least the reasons described above in Count XXIII, the claims of the '827 patent are invalid. Plaintiffs cannot be held liable for infringement of invalid patent claims.

304. Plaintiffs are therefore entitled to a judicial declaration that their making, using, selling, offering to sell, or importing vadadustat has not infringed and will not infringe any valid claim of the '081 patent.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request that judgment be entered:

A. Declaring that all claims of the patents-in-suit are invalid for failure to satisfy one or more of the conditions for patentability specified in Title 35 of the United States Code and related judicial doctrines, including but not limited to 35 U.S.C. §§ 101, 102, 103, and/or 112 and/or obviousness-type double patenting;

B. Declaring that the making, using, selling, offering for sale, or importation of vadadustat by Plaintiffs has not infringed and will not infringe, either directly or indirectly, any valid claim of the patents-in-suit, either literally or under the doctrine of equivalents;

C. If the facts demonstrate that the case is exceptional within the meaning of 35 U.S.C. § 285, awarding to Plaintiffs their reasonable attorneys' fees, expenses, and disbursements of this action;

D. Awarding to Plaintiffs their reasonable costs and expenses in this action; and

E. Awarding Plaintiffs any other remedy or relief to which they may be entitled and which the Court deems appropriate.

Dated: March 29, 2021

Respectfully submitted,

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